Acta Genetica et Statistica Medica

Condidit: **Gunnar Dahlberg** †

Vol. 9, No. 1 1959

BASEL (Schweiz) S. KARGER NEW YORK

Printed in Switzerland

INDEX

Beckman, L.; Broman, B.; Jonsson, B. and Mellbin, T.: Acta genet. *9* : 1—8 (1959)

FURTHER DATA ON THE BLOOD GROUPS OF THE SWEDISH LAPPS

By

L. BECKMAN[1], B. BROMAN[2], B. JONSSON[2] and T. MELLBIN[3]

1. Introduction

The Lapps are anthropometrically distinct from other Swedish populations as characterized by their low stature, broad heads and a markedly dark pigmentation.

Blood group investigations of the Norwegian Lapps *(Allison et al.*, 1952) and the Swedish Lapps (*Allison et al.*, 1956) have clearly shown that also their serological traits are quite distinctive. The most prominent features were very high A_2-frequency, low frequency of Rh-negative individuals and low K-, M- and P-frequencies. Some differences between the Norwegian and Swedish Lapps (*Allison et al.*, 1956) were found, but no significant differences between Swedish Lapps speaking the south and central Lappish languages respectively.

2. Present Investigation

The present investigation comprised the children in all Swedish nomad schools. The samples from Norrbotten county were collected during the autumn of 1957 by *Mellbin* and from the southern schools by *Beckman.* The typing was made by Broman and Jonsson.

The fact that the individuals of this investigation belong to nomad schools implies that practically all of them are genuine Swedish nomad

[1] State Institute for Human Genetics, Uppsala. [2] Blood Group Serological Department, State Laboratory for Forensic Chemistry, Stockholm. [3] Department of Pediatrics, University Hospital, Uppsala.

Lapps. This should be kept in mind when comparing the results with earlier investigations of Swedish Lapps.

The individuals have been grouped into five regional groups (cf. the map). In Norrbotten county the classification has been made according to the parish of birth. All individuals born south of Jokkmokk have been grouped together.

The blood group distributions are shown in table 1–6. Gene frequencies have been calculated by the methods recommended by *Mourant* (1954).

In this investigation the A_2-frequency is higher than in earlier investigations. There is a continous decrease of A_2-frequencies towards the north. The 0-frequencies of Jukkasjärvi–Karesuando are higher than those of the southern regions ($\chi^2 = 4.41$, 1 d.f., $0{,}05 > P > 0.02$). The frequencies of the A_1- and B-genes show no significant variations.

As in the earlier investigations the frequency of Rh-negative individuals is low.

No considerable heterogeneity was obtained for the D-frequency. The frequencies of the C-gene ($\chi^2 = 16.31$, 4 d.f., $0.01 > P > 0.001$) and the E-gene ($\chi^2 = 14.13$, 4 d.f., $0.01 > P > 0.001$), however, show heterogeneity, and a still higher heterogeneity is demonstrated by the C^W-gene ($\chi^2 = 38.55$, 4 d.f., $P > 0.001$). The C^W-frequency is, in this material, remarkably high. In the southernmost group, which corresponds roughly to the area where the south Lappish language is spoken, the C^W-frequency is significantly lower.

The frequency of the cDE-chromosome is not especially high in the Swedish Lapps. The paper by *Allison et al.* (1956) contained two different series – the main series and the Vittangi nomads. The main series is different from the Vittangi series and most of our samples, which show high CD-frequencies and low CDE- and DE-frequencies. It is likely that the disagreements between the main series and our data are due to the fact that the former material is more mixed (the main series is described in the following way: "... most were settled forest workers and some were nomads...").

Low M-frequencies were found in all samples but one (the southernmost sample). The difference between this sample and the other samples is significant ($\chi^2 = 16.81$, 1 d.f., $P > 0.001$). The higher value obtained in the southern sample indicates an intermixing with the surrounding populations.

The P-frequencies are low except for the Karesuando sample where they agree with those of the Norwegian Lapps and those of the non-Lappish population of Norrbotten county. The difference between the Karesuando

sample and the other samples is significant ($\chi^2 = 5.28$, 1 d.f., $0.05 > P > 0.02$).

Map 1. The regional location of the different groups of Swedish Lapps (the numerals refer to the Tables).

Table I A_1A_2B0 Groups and Gene Frequencies

Region	A_1	A_2	B	A_1B	A_2B	0	n	χ^2	p_1	p_2	q	r	p+q+r
1 Jämtl., Västerb., Arjeplog	14	69	4	1	2	28	118	0.34	6.6	42.2	3.0	48.2	100.65
2 Jokkmokk	7	44	1	0	0	19	71	0.74	5.1	42.0	0.7	52.2	99.43
3 Gällivare	6	27	2	3	0	11	49	0.002	9.6	38.8	5.2	46.4	100.11
4 Jukkasjärvi	12	61	6	0	4	40	123	0.03	5.0	33.9	4.0	57.1	99.83
5 Karesuando	8	26	2	0	1	21	58	0.03	7.2	29.9	2.6	60.3	99.81
Total data	47	227	15	4	7	119	419	0.05	6.3	37.2	3.1	53.4	99.87

Table II Rh Groups

Region	CCD	C^wCD	CcD	C^wcD	CcDE	CwcDE	DEE	DEe	D	C	E	Rh—	n
1 Jämtl., Västerb., Arjeplog	35	1	32	6	13	1	2	12	7	0	0	9	118
	29.66	0.85	27.12	5.08	11.02	0.85	1.69	10.17	5.93	0.00	0.00	7.63	100.00
2 Jokkmokk	15	11	19	5	10	1	0	5	1	0	0	4	71
	21.14	15.49	26.76	7.04	14.08	1.41	0.00	7.04	1.41	0.00	0.00	5.63	100.00
3 Gällivare	22	3	3	1	11	1	2	3	1	0	0	2	49
	44.91	6.12	6.12	2.04	22.45	2.04	4.08	6.12	2.04	0.00	0.00	4.08	100.00
4 Jukkasjärvi	30	24	33	16	12	1	0	2	2	0	0	3	123
	24.39	19.51	26.83	13.01	9.75	0.81	0.00	1.63	1.63	0.00	0.00	2.44	100.00
5 Karesuando	13	5	16	7	1	2	0	6	3	0	0	5	58
	22.42	8.62	27.59	12.07	1.72	3.45	0.00	10.34	5.17	0.00	0.00	8.62	100.00
Total data	115	44	103	35	47	6	4	28	14	0	0	23	419
	27.45	10.50	24.58	8.35	11.22	1.43	0.96	6.68	3.34	0.00	0.00	5.49	100.00

Only one Kell-positive individual was found. He belonged to the southernmost sample. A very low frequency has been reported earlier. It seems likely that the pure Lapps lack the Kell-antigen entirely.

Among 220 individuals no Diego-positives were found.

Table III

Chromosome Frequencies

Region	CDe	$C^{w}De$	cDE	cDe	cde	n
1 Jämtl., Västerb., Arjeplog	49.1	3.4	12.7	8.7	26.1	118
2 Jokkmokk	49.3	12.0	11.3	2.0	25.4	71
3 Gällivare	62.2	5.1	19.4	2.4	10.9	49
4 Jukkasjärvi	52.4	16.7	6.1	5.6	19.2	123
5 Karesuando	41.4	12.1	7.8	8.1	30.6	58
Total data	50.6	10.1	10.6	6.1	22.6	419
Allison et al., 1956 Swedish Lapps	49.1	4.3	23.8	2.7	20.1	193
Allison et al., 1952 Norwegian Lapps	48.6	3.9	18.4	10.3	18.8	183

Table IV

Frequency of Rh-genes

Region	D	d	C	C^{w}	c	E	e	n
1 Jämtl.,Västerb., Arjeplog	72.4	27.6	49.1	3.4	47.5	12.7	87.3	118
2 Jokkmokk	76.3	23.7	49.3	12.0	38.7	11.3	88.7	71
3 Gällivare	79.8	20.2	62.2	5.1	32.7	19.4	80.6	49
4 Jukkasjärvi	84.4	15.6	52.4	16.7	30.9	6.1	93.9	123
5 Karesuando	76.6	29.4	41.4	12.1	46.5	7.8	92.2	58
Total data	77.1	22.9	50.6	10.1	39.3	10.6	89.4	419

Table V

MN Groups and Gene Frequencies

Region	MM	MN	NN	n	M	N
1 Jämtl.,Västerb.,Arjeplog	38	59	21	118	57.2	42.8
	32.20	50.00	17.80	100.00		
2 Jokkmokk	13	44	14	71	49.3	50.7
	18.31	61.97	19.72	100.00		
3 Gällivare	4	27	18	49	35.7	64.3
	8.16	55.10	36.73	99.99		
4 Jukkasjärvi	15	65	43	123	38.6	61.4
	12.20	52.85	34.95	100.00		
5 Karesuando	11	28	19	58	43.1	56.9
	18.97	48.27	32.76	100.00		
Total data	81	223	115	419	45.94	54.06
	19.33	53.22	27.45	100.00		

Table VI

P Groups and Gene Frequencies

Region	P+	%	P—	%	n	P	p
1 Jämtl., Västerb., Arjeplog	72	61.02	46	38.98	118	37.6	62.4
2 Jokkmokk	46	64.79	25	35.21	71	40.7	59.3
3 Gällivare	26	53.06	23	46.94	49	31.5	68.5
4 Jukkasjärvi	73	59.35	50	40.65	123	36.2	63.8
5 Karesuando	44	75.86	14	24.14	58	50.9	49.1
Total data	261	62.29	158	37.71	419	38.6	61.4

3. Conclusion

The present investigation has shown that the "purest" Lapps are probably found among the Swedish nomads. The C^W-gene as well as the A_2-gene seem to be typical of this Lapp group. There is, however, no exact

agreement between the occurrence of high A_2- and C^W-frequencies, which might be expected. From the very low 0-frequency in the Norwegian Lapps a decrease of the 0-frequency towards the north might be expected in the Swedish samples. The reverse was found.

There are significant regional variations in the AB0-, Rh-, MN- and P-systems, indicating a considerable heterogeneity within the Swedish Lapp population. The group speaking the south Lappish dialect has higher M- and lower 0- and C^W-frequencies than the group speaking central Lappish. Genetic drift may be responsible for part of the variations found between the Swedish Lapp populations. However, the peculiar blood group frequencies demonstrated by all Lapps are unlikely to have originated through genetic drift only. As the Lapps are thought to have lived isolated for a very long period of time, some of their genetic peculiarities might be tentatively explained by long time selection against heterozygotes through serological incompatibility.

Summary

Blood group data for the AB0, Rh, MN, P, Kell and Diego systems are presented for 419 Swedish nomadic Lapp children. Significant regional variations have been demonstrated in the AB0, Rh-, MN- and P-systems.

Zusammenfassung

Es werden Blutgruppendaten für das AB0-, Rh-, MN-, Kell- und Diego-System bei 419 schwedisch-nomadischen Lappenkindern vorgelegt. Signifikante regionale Unterschiede konnten für das AB0-, Rh-, MN- und P-System dargestellt werden.

Résumé

Les auteurs exposent les résultats des examens des groupes sanguins AB0, Rh, MN, P, *Kell* et *Diego* trouvés chez 419 enfants de Lapons nomades suédois. Des variations régionales significatives ont été enregistrées pour les systèmes AB0, Rh, MN et P.

ACKNOWLEDGEMENTS

We are indebted to Dr. M. Layrisse, Caracas, Venezuela, for supplying Dr. B. Broman with a very potent anti Di^a-serum. Dr. L. Beckman is in receipt of grants from the Swedish Natural Science Research Council.

LITERATURE

Allison, A. C.; Hartmann, O.; Brendemoen, O. I. and Mourant, A. E.: The blood groups of the Norwegian Lapps. Acta path. microbiol. scand. *31:* 334–338 (1952).

Allison, A. C.; Broman, B.; Mourant, A. E. and Ryttinger, L.: The blood groups of the Swedish Lapps. J. roy. anthrop. Inst. *86/I:* 87–94 (1956).

Boyd, W. C.: Blood groups. Tab. Biol. *17:* 113–240 (1939).

Collinder, B.: The Lapps, p. 252 (Princeton University Press; Priceton 1949).

Dahlberg, G. and Wahlund, S.: The race biology of the Swedish Lapps. Part 2. Anthropometrical survey (Almquist and Wiksell, Uppsala 1941).

Lundman, B.: On the origin of the Lapps. Physico-anthropological observations. Ethnos, Stockh. *11:* 71–88 (1946).

Lundman, B.: Ergebnisse der anthropologischen Lappenforschung. Anthropos *47:* 119 bis 132 (1952).

Lundman, B.: Publications on the physical anthropology of the Lapps. Arctica, Stud. ethnograph. Upsaliensia *11:* 277–284 (1956).

Mourant, A. E.: The distribution of the human blood groups (Blackwell Scientific Publications, Oxford 1954).

Race, R. R. and Sanger: Blood groups in man (Blackwell Scientific Publications, Oxford 1956).

Authors' addresses: Dr. B. Broman and B. Jonsson, Statens rättskemiska laboratorium, *Stockholm;* fil. lic. Lars Beckman, Statens rasbiologiska Institut, *Uppsala*, and Dr. T. Mellbin, Pediatriska Kliniken, Akademiska Sjukhuset, *Uppsala* (Sweden).

Beckman, L.: Acta genet. *9* : 9—17 (1959)

From the State Institute for Human Genetics, Uppsala

THE FREQUENCY OF REGIONAL INTRAMARRIAGE IN NORTH SWEDEN

By LARS BECKMAN

The frequency of marriages between individuals belonging to the same or different populations is modified in many ways. Factors such as the size of the area and the population density influence the intramarriage frequency. When using data from the official statistics, one is forced to work with administrative subdivisions of different size and population density. Therefore such data are always more or less biased.

I have made an analysis of the geographical variation of intramarriage frequencies in north Sweden using data from the primary files of the anthropometric survey of Swedish conscripts by *Lundborg* and *Linders* (1926). In this survey, data on the birth-parish of the father and mother of nearly all examined conscripts were collected, but have not been analysed before. Unpublished data collected later by *Lundborg* were also used. From the six northernmost counties of Sweden (see map 1 and table 1) 9, 547 marriage combinations contracted approximately between 1880 and 1900 were recorded and distributed over 107 subregions. Sometimes a subregion consists of one parish, but in most cases it is composed of many parishes. Some data on Norrbotten county have been presented previously (*Beckman*, 1957).

The analysis of the variation within and between counties is shown in table 2. The counties of Norrbotten, Västernorrland and Kopparberg, show highly significant variations of intramarriage frequencies. The county of Jämtland is more homogeneous. Map 2 shows the main features of variation for the intramarriage frequency using a combined isarithm- and raster technique.

Map 1. Regional subdivisions of Sweden.
The numerals of the map refer to Table 1.

An interesting problem is whether the variations are due mainly to different degrees of isolation or if they are merely a result of different sizes of the subregions or of different densities of population. Table 3 gives information of the relation between intramarriage frequency and the size of the region. As expected, there is a significant rise of intramarriage frequency with the increasing size of the area. Furthermore, there is a significant increase of intramarriage frequency with the decreasing density of the

Table I

Size of Area, Density of Population and Frequency of Marriages between Individuals Born in the Same Area

I. Norrbotten county

Region	Area, sq. kms.	Density of population inh./sq. km.	Both partners from the same region, %	Total
1	5 678	0.92	61.4	166
2	12 967	0.18	56.7	67
3	18 143	0.24	36.6	88
4	15 995	0.73	59.3	134
5	19 446	0.22	62.5	80
6	3 015	5.95	58.8	352
7	1 726	2.89	55.8	138
8	1 106	19.58	54.3	210
9	1 830	7.55	54.8	306
10	2 022	3.85	62.8	223
11	1 717	7.54	69.1	226
12	2 779	1.99	72.3	169
13	875	8.03	43.7	126
14	2 379	2.26	44.8	143
15	1 499	1.33	36.7	49
16	2 885	0.84	56.5	69
17	3 513	0.83	53.5	101

II. Västerbotten county

1	2 906	1.10	47.5	40
2	8 166	0.81	52.1	94
3	4 010	0.73	52.9	70
4	3 475	0.34	54.5	11
5	7 409	0.39	60.9	46
6	4 372	1.25	50.0	84
7	5 613	1.44	50.9	169
8	1 667	1.51	47.2	53
9	1 561	6.24	55.2	105
10	1 825	5.22	57.3	110
11	1 090	18.63	44.4	126
12	2 793	2.65	44.4	90
13	753	4.37	38.3	47
14	1 276	7.46	58.3	96
15	1 851	4.46	39.6	96
16	808	5.14	60.0	80
17	1 342	1.37	60.1	238
18	1 077	8.16	50.0	100
19	1 718	2.86	41.8	98
20	1 734	2.20	40.6	64

III. Västernorrland county

Region	Area, sq. kms.	Density of population inh./sq. km.	Both partners from the same region, %	Total
1	1 951	4.09	49.2	65
2	1 654	7.81	59.2	103
3	711	13.10	41.5	65
4	413	61.05	43.6	126
5	307	34.45	41.7	60
6	1 885	4.79	49.3	71
7	778	15.43	44.3	88
8	666	22.80	44.9	127
9	709	20.11	55.7	131
10	1 873	4.47	66.1	62
11	1 611	7.35	40.7	86
12	1 521	7.53	45.9	111
13	1 027	15.71	47.8	157
14	1 078	12.30	68.6	105
15	3 698	3.00	62.4	125
16	1 981	2.71	58.4	77
17	1 575	3.00	71.0	38

IV. Jämtland county

1	4 558	0.76	47.4	38
2	4 158	1.34	39.6	53
3	4 128	2.44	41.1	90
4	3 666	2.84	44.5	128
5	1 963	5.70	38.6	127
6	2 939	3.97	50.0	120
7	879	12.52	32.3	65
8	2 095	2.50	42.9	56
9	2 579	3.55	44.9	89
10	4 045	1.37	31.3	32
11	7 432	0.62	56.2	46
12	3 009	2.78	46.8	79
13	6 205	1.26	51.1	88

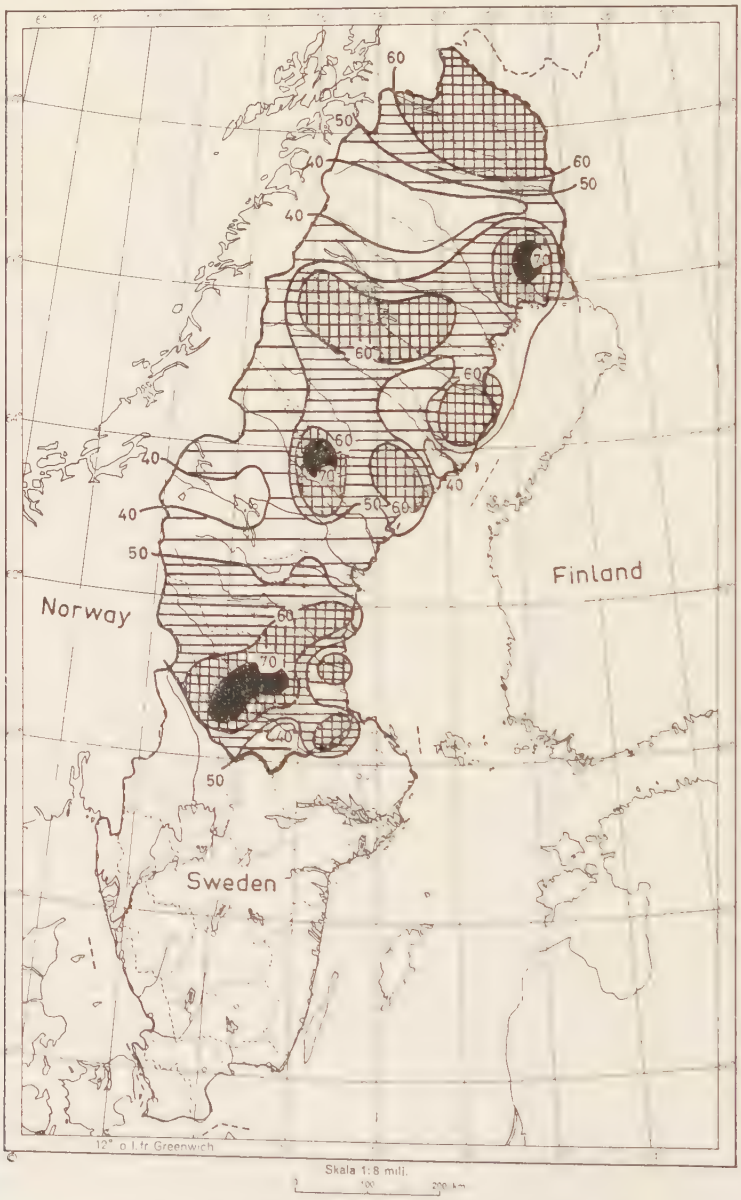
V. Gävleborg county

1	755	11.80	61.1	72
2	1 156	16.62	52.0	123
3	847	59.08	34.3	131
4	346	12.30	39.1	23
5	999	7.22	49.2	61
6	739	10.90	60.8	51
7	815	13.82	54.5	55

Region	Area, sq. kms.	Density of population inh./sq. km.	Both partners from the same region, %	Total
8	930	5.97	45.8	24
9	939	6.09	50.0	28
10	792	23.81	49.3	75
11	493	10.60	46.1	26
12	728	14.02	62.1	66
13	696	10.23	65.5	29
14	1 807	4.11	61.5	39
15	1 819	6.30	41.7	36
16	1 727	7.36	55.6	72
17	1 070	19.10	61.7	94
	VI. Kopparberg county (Dalecarlia)			
1	4 369	0.49	50.0	18
2	2 392	1.94	60.5	38
3	2 476	1.98	58.5	41
4	2 174	6.22	65.4	107
5	2 397	3.23	68.4	57
6	1 738	3.16	59.5	42
7	891	3.40	66.7	30
8	1 033	10.02	77.4	53
9	1 062	11.88	70.7	106
10	1 081	6.37	72.7	44
11	1 447	7.14	57.7	85
12	889	16.96	46.7	105
13	441	18.81	34.7	75
14	508	10.59	36.1	36
15	290	17.87	52.9	34
16	401	19.19	72.8	81
17	601	26.49	40.7	86
18	522	39.14	34.6	81
19	1 415	7.09	71.9	64
20	309	18.37	36.7	49
21	368	14.78	54.2	59
22	1 441	16.44	42.0	131
23	238	17.49	43.8	48

population (table 4). This is also to be expected as there is an association between the size of the area and the population density. The associations demonstrated above refer, however, to the entire area and exceptions are found. In Dalecarlia, e.g., with rather small regions, there is a concen-

tration of regions with high intramarriage frequencies. Thus, in spite of the source of error depending on different size and population densities of the areas, we might tentatively conclude that part of the heterogeneities



Map 2. Isarithms for intramarriage in the investigation area.

Table II

Analysis of the Heterogeneity of the 107 Areas in Respect to the Frequency of Intramarriages

Variation	D. of F	χ^2	P
Within Norrbotten county	16	43.94	< 0.001
Within Västerbotten county	19	35.26	$0.02 > P > 0.01$
Within Västernorrland county	16	52.61	< 0.001
Within Jämtland county	12	14.88	$0.30 > P > 0.20$
Within Gävleborg county	16	34.85	$0.01 > P > 0.001$
Within Kopparberg county	22	116.39	< 0.001
Between counties	5	63.50	< 0.001
Between all areas	106	361.94	< 0.001

Table III

The Relation between Intramarriage Frequency and Size of the Area

Intramarriages %	Area square kms. —1000	1000—2000	2000—	Number of regions
50–100	12	24	24	60
0– 49	21	15	11	47
Total	33	39	35	107

Heterogeneity: $\chi^2 = 7.90$, 2 d.f., $0.02 > P > 0.01$

Table IV

The Relation between Intramarriage Frequency and Density of Population

Intramarriages %	Density of population inh./square km. —5	5—10	10—	Number of regions
50–100	30	25	5	60
0– 49	19	13	15	47
Total	49	38	20	107

Heterogeneity: $\chi^2 = 9.78$, 2 d.f., $0.01 > P > 0.001$

found in the counties of Norrbotten, Västernorrland and Kopparberg may depend on differences in the breeding structure of the populations.

If the view is accepted that a high frequency of intramarriages is a measure of the relative isolation of the population in question. it may be inquired whether there is any agreement between the pattern of intramarriages and the occurrence of isolated populations as judged from anthropological and demographical data.

If the areas in Norrbotten with high intramarriage frequencies, *Böök* (1953 and 1956) and *Böök* and *Kostmann* (1956) have made population investigations showing that the areas in question are geographical isolates. In the parish of Överkalix, which has the highest intramarriage frequency of Norrbotten, *Kostmann* has demonstrated the accumulation of a rare, genetically determined recessive disease. This may be due to inbreeding.

Dalecarlia, which shows a high frequency of intramarriages. is characterized by a special structure of settlement giving rather sharp social and biological borders between different parishes or even villages (cf. *Frödin*, 1933; *Erixon*, 1938; *Lundman*, 1945).

Summary

This report on intramarriage data from North Sweden shows some agreements with demographical and anthropological data. but due to the sources of error introduced by comparing areas of different size and population density, conclusions based on the statistical analysis must be guarded. As this report deals with data on parents to conscripts doing their military service about 1923. it can be said to reflect the pattern of intramarriages at the turn of the century.

Zusammenfassung

Dieser Bericht über die durchschnittliche Heiratshäufigkeit innerhalb des gleichen Gemeindeverbandes in Nordschweden zeigt eine gewisse Übereinstimmung mit demografischen und anthropologischen Daten; jedoch müssen wegen der Fehlerquellen. die sich beim Vergleich von Gebieten verschiedener Größe und Bevölkerungsdichte ergeben. Schlußfolgerungen. die auf statistischer Analyse aufgebaut sind. mit gewisser Zurückhaltung betrachtet werden. Da dieser Bericht Daten von Eltern Wehrpflichtiger behandelt. die etwa 1923 ihren Militärdienst leisteten. so vermittelt er praktisch ein Bild über die Verteilung von Heiraten innerhalb des gleichen Gemeindeverbandes um die Jahrhundertwende.

Résumé

Cette étude sur les unions consanguines dans la Suède du nord montre une certaine concordance avec les données démographiques et anthropologiques. Cependant, vu les sources d'erreur introduites par la comparaison de régions différentes par leur grandeur et leur densité de population, les conclusions fondées sur l'analyse statistique méritent une certaine réserve. Comme cette enquête se base sur les parents de recrues, qui ont fait leur service militaire autour de 1923, on peut admettre que les résultats obtenus reflètent bien le système endogamique tel qu'il était au début du siècle.

LITERATURE

Beckman, L.: A contribution to the genetical demography of North Sweden. – Eugen Quart. *4:* 153–156 (1957).

Böök, J.A.: A genetic and neuropsychiatric investigation of a North-Swedish population. – Acta genet. *4:* 1–100, 133–139 and 345–414 (1953).

Böök, J.A.: Genetical investigations in a North Swedish population. – Ann. hum. Genet. *20:* 239–250 (1956).

Böök, J.A. and Kostmann, R.: Genetic aspects of infantile agranulocytosis.– Acta paediat., Stockh., Suppl. *105*, pp. 64–72 (1956).

Erixon, S.: Svenskt folkliv. (J. A. Lindblads Förlag, Uppsala 1938).

Frödin, J.: Den nord- och mellansvenska byn. – Bidr. till Bondesamfundets hist., II (Oslo 1933).

Lundborg, H. and Linders, F. J.: The racial characters of the Swedish nation (Almquist & Wiksell, Uppsala 1926).

Lundman, B.: Dala-allmogens antropologi (Almquist & Wiksell, Uppsala 1945).

Author's address: L. Beckman, Statens rasbiologiska Institut, *Uppsala* (Sweden)

Wendt, G. G.: Acta genet. *9*: 18—32 (1959)

Aus der Diätendozentur für Anthropologie (Dozent Dr. Wendt) am Anatomischen Institut (Dir.: Prof. Dr. Niessing) der Philipps-Universität Marburg (Lahn)

DAS ERKRANKUNGSALTER BEI DER HUNTINGTONSCHEN CHOREA[1]

Von G. G. WENDT

unter Mitwirkung von

H. J. LANDZETTEL und I. UNTERREINER

I. Problemstellung

Aus den größeren zusammenfassenden Arbeiten über die Huntingtonsche Chorea sind in Tab. I die Durchschnittswerte für das Erkrankungsalter zusammengestellt. Man kann sich nach diesen Daten die Meinung bilden, die Chorea beginne durchschnittlich etwa zwischen 35 und 40 Jahren. Diese Meinung hat auch ihren Niederschlag in der Literatur gefunden.

Tab. I. Durchschnittliches Erkrankungsalter bei der Huntingtonschen Chorea

Durchschnittliches Erkrankungsalter	Zahl der Fälle	Autor
37,8	138	Davenport und Muncey (1916)
38,1	323	Entres (1921)
37,1	218	Hughes (1925)
35,51	460	Bell (1934)
41,1	35	Sjögren (1936)
36,19	446	Panse (1942)
35,3	204	Reed (1958)

[1] Mit Unterstützung der Deutschen Forschungsgemeinschaft durchgeführte Sammlung aller Fälle von Huntingtonscher Chorea aus der Bundesrepublik: 1. Mitteilung.

Tatsächlich geben aber die Werte in Tab. I nicht das durchschnittliche Erkrankungsalter bei der Huntingtonschen Chorea an, sondern das durchschnittliche Erkrankungsalter der von den einzelnen Autoren verwerteten Fälle. Zwischen beiden Angaben kann ein erheblicher Unterschied bestehen. In den bisherigen Veröffentlichungen benutzten die Verfasser zur Frage des Erkrankungsalters jeweils ihr gesamtes Material. Dabei werden aber aus den dem Erhebungszeitpunkt näher gelegenen Jahrgängen zwar schon die früh erkrankten, nicht aber die spät erkrankenden Choreatiker erfaßt sein. Der Durchschnittwert liegt also zu niedrig.

Diese Überlegungen hauptsächlich haben uns veranlaßt, das Erkrankungsalter am eigenen Material besonders zu bearbeiten.

II. Material und Erfassungsmethode

Einer Anregung von *H. Nachtsheim* folgend, hat *Wendt* seit fast drei Jahren sich bemüht, alle Fälle von Huntingtonscher Chorea aus dem Gebiet der Deutschen Bundesrepublik mit ihren Stammbäumen zu sammeln. Dabei wurden bis zum Herbst 1958 rund 5000 choreatische Krankheitsfälle mit mehr als 10 000 gesunden oder noch gesunden Verwandten karteimäßig, in ihren familiären Zusammenhängen, in ausführlichen Krankenblattauszügen und eigenen Untersuchungsbefunden registriert. Die Erfassung dieses Materials geht aus von den Fällen der deutschen Kliniken und Heilanstalten. Sie begnügt sich jedoch nicht mit den gegenwärtig dort behandelten Patienten, sondern erarbeitet auch aus den zumeist erhaltenen Archiven alle erreichbaren Akten. Im allgemeinen wurden die seit dem ersten Weltkrieg behandelten Fälle herausgesucht, teilweise konnten auch noch ältere Akten berücksichtigt werden.

Ferner wurden von den praktischen Nervenärzten Deutschlands und von den Gesundheitsämtern die dort bekannt gewordenen Krankheitsfälle erfragt. Dieses Stadium der Erfassung ist heute im wesentlichen abgeschlossen.[1] Zurzeit werden nun durch äußerst umfangreiche Anfragen bei Meldeämtern, Standesämtern und Pfarrämtern die Stammbäume aufgestellt, bzw. vervollständigt. In einem – ebenfalls schon angelaufenen – dritten Arbeitsgang werden jetzt die so als Blutsverwandte eines Choreatikers

[1] Den Direktoren der deutschen Nervenkliniken und Heilanstalten, den deutschen Nervenärzten und den Leitern vieler Gesundheitsämter sind wir für freundliche Hilfe zu großem Dank verpflichtet. Auch muß erwähnt werden, daß wir durch freundliches Entgegenkommen der deutschen Forschungsanstalt für Psychiatrie in München (Genealogische Abteilung, Prof. Wagner) ein großes Material einbeziehen konnten, das *Entres* bis zu seinem Tode gesammelt und bereits in Stammbäumen geordnet hatte.

erfaßten Personen, soweit sie noch leben, nachuntersucht. Bei verstorbenen Verwandten wird durch Beschaffung des Totenscheines, Rücksprache mit den behandelnden Ärzten und mit lebenden Angehörigen die Frage geklärt, ob ebenfalls eine Chorea bestand. Dieses Vorgehen scheint uns Gewähr dafür zu bieten, daß nach Abschluß der Erhebungen praktisch alle deutschen Huntington-Sippen erfaßt sind. Auf einzelne Schwierigkeiten und die Wege zu ihrer Überwindung kann in diesem Zusammenhang nicht eingegangen werden.

Hier sei noch betont, daß also nicht nur rückschauend Stammbäume der heute lebenden Kranken aufgestellt wurden, sondern daß in gleichem Ausmaß gegenwärtige Huntington-Fälle, die oft noch nicht in Behandlung waren, als Kinder oder Enkel früherer Ausgangsfälle erfaßt wurden.

Von den bei uns heute registrierten 5000 choreatischen Krankheitsfällen wurden bisher 3600 als sichere Fälle von Huntingtonscher Chorea bestätigt.

Für die hier interessierende Frage des Erkrankungsalters konnten die Daten von 1473 Huntington-Fällen verwandt werden. Diese Zahl ist zufällig bestimmt als die Anzahl derjenigen Fälle, von denen uns beim Zeitpunkt der Auswertung verläßliche Informationen über das Erkrankungsalter vorlagen.

III. Die Definition des Erkrankungsalters

Zum Krankheitsbild der Huntingtonschen Chorea gehören neben den charakteristischen neurologischen Symptomen auch recht unterschiedliche psychische Veränderungen. Diese Veränderungen können zusammen mit den neurologischen Symptomen beginnen, können den ersten neurologischen Symptomen folgen, eventuell wohl auch einmal ausbleiben. Sie können aber auch mehr oder weniger lange Zeit vor den ersten neurologischen Erscheinungen auftreten. In unserem Material befinden sich z.B. mehrere sichere Fälle Huntingtonscher Chorea, die zunächst jahrelang klinisch als Psychopathie, Schizophrenie oder Debilität angesehen wurden.

Als Erkrankungsalter muß man zweifellos dasjenige Lebensalter ansehen, in dem die ersten (psychischen oder neurologischen) Symptome auftraten. Nun beginnt die Chorea schleichend. Besonders hinsichtlich der psychischen Symptome ist die Grenze zwischen «noch normalen» und «schon krankhaften» Zuständen oft nur schwer zu ziehen. Aber auch der Übergang von etwa allgemeiner «Nervosität» zu eindeutiger Unruhe ist selbst bei klinischer Beobachtung zumeist nicht auf einen Monat genau festzulegen.

In zahlreichen Krankengeschichten findet sich anamnestisch die Angabe eines akuten Krankheitsbeginnes – meist in Zusammenhang mit einem psychischen oder somatischen Trauma. Einer genauen Nachforschung halten diese Angaben, die dem Kausalitätsbedürfnis der Kranken oder ihrer Angehörigen entspringen, höchst selten stand.

Schon wegen des schleichenden Auftretens der Symptome ist also die Bestimmung des Erkrankungsalters schwierig. Auch muß man, wie *Panse* betont, oft erst rückschauend – nach voller Ausprägung des Krankheitsbildes – den Beginn der Krankheit festlegen. Besonders unsicher scheint uns die Bestimmung des Erkrankungsalters in den Fällen zu sein, in denen psychische Veränderungen den neurologischen Symptomen vorausgehen. *Reed* (1958) hat aus diesen Erwägungen heraus das Erkrankungsalter als den Beginn der choreatischen Bewegungsunruhe (onset of choreiform movement) definiert. Der Beginn choreatischer Unruhe ist möglicherweise relativ sicherer festzustellen. Er kann aber nicht generell als Krankheitsbeginn gelten, denn viele Choreatiker werden lange vor dem Auftreten neurologischer Symptome schon wegen psychischer Veränderungen auffällig oder behandlungsbedürftig.

Für das hier vorgelegte Material wird an der von *Panse* gegebenen Definition des Erkrankungsalters festgehalten:

«Als Beginn des Leidens ist nicht das erstmalige Erkennen der choreatischen Störungen angesetzt worden, sondern jeweils das erste Hervortreten von psychischen oder neurologischen Auffälligkeiten, die rückschauend bereits als Ausdruck des choreatischen Prozesses angesehen werden mußten.»

Die in Tabelle I neben *Panse* zitierten Autoren haben zwar – mit Ausnahme von *Reed* – die Definition des Erkrankungsalters nicht diskutiert. Sie sehen jedoch offenbar auch das erste Auftreten psychischer oder neurologischer Symptome als Krankheitsbeginn an.

Aus Tabelle I ergibt sich, daß *Reed* von allen Untersuchern den niedrigsten Durchschnittswert für das Erkrankungsalter fand. Dies ist besonders auffällig, da in seinem Material Krankheitsfälle, die zunächst psychische Erscheinungen zeigten, erst später, beim Beginn der choreatischen Unruhe, erfaßt worden sind. Drei Erklärungsmöglichkeiten bieten sich an:

Einmal könnten *Reed* und seine Mitarbeiter tatsächlich wesentlich genauere Feststellungen getroffen haben als alle früheren Untersucher. Es könnte ihnen so gelungen sein, häufiger die frühesten Krankheitssymptome zu erfassen.

Zum anderen könnten *Reed* und seine Mitarbeiter in dem Bestreben, möglichst die frühesten Symptome zu registrieren, zu weit gegangen sein.

Es ist bekannt, daß in vielen Huntington-Sippen eine allgemeine Nervosität zu beobachten ist. Wir wissen aus eigener Erfahrung, wie man bei intensiver Befragung von Angehörigen nicht selten Zeichen dieser allgemeinen Nervosität als ganz unglaubwürdig frühe Krankheitssymptome geschildert bekommt.

Schließlich könnte auch zwischen dem Material von *Reed* und dem Material der anderen Untersucher ein echter Unterschied hinsichtlich des durchschnittlichen Erkrankungsalters bestehen.

Es läßt sich nicht entscheiden, welche der vorstehenden Erklärungsmöglichkeiten zutrifft. Auf alle Fälle aber ist der «Beginn choreatischer Unruhe» im Gegensatz zum Erkrankungsalter (nach *Panse*) ein nur theoretisch interessanter Wert. Dies wird noch unterstrichen dadurch, daß es nicht nur Huntington-Fälle gibt, die zunächst jahrelang nur psychisch verändert sind, sondern auch Fälle, bei denen nicht eine choreatische Unruhe, sondern eine Versteifung das Krankheitsbild bestimmt.

Es war schon erwähnt, daß wir von 3600 Huntington-Fällen nur 1473 zur Frage des Erkrankungsalters herangezogen haben. Es sind das diejenigen Fälle, in denen von dritter Seite, also nicht vom Kranken selbst, offensichtlich zuverlässige Angaben über die Vorgeschichte und den Krankheitsbeginn vorlagen. Wir glauben daher, daß für jeden der von uns verwerteten Fälle das Erkrankungsalter mit größtmöglicher Genauigkeit bestimmt ist.

IV. Eigene Befunde

Auf den ersten Blick erscheint die Bestimmung des durchschnittlichen Erkrankungsalters als eine recht einfache Sache: Man errechnet den Durchschnitt aus dem Erkrankungsalter der zur Verfügung stehenden Fälle. So wird ja zumeist das mittlere Erkrankungsalter berechnet und so sind auch die in Tabelle I zusammengefaßten Autoren bezüglich der Chorea Huntington vorgegangen.

Verfahren wir so auch hinsichtlich der eigenen 1473 Fälle, dann erhalten wir 40,18 Jahre als Durchschnittswert (Tab. II). Der Wert liegt an der oberen Grenze der bisherigen Angaben (Tab. I). Dies erklärt sich wahrscheinlich dadurch, daß in unserem Material, das ja in das vorige Jahrhundert hineinreicht, der Anteil heute abgeschlossener Generationen größer ist, als bei den anderen Autoren. Die Geburtsjahrgänge 1800 bis 1899 stellen zirka $^2/_3$ unseres Materials. Die entsprechend weit vor dem Erfassungszeitpunkt liegenden Geburtsjahrgänge in der Veröffentlichung von *Panse* z. B. stellen nur zirka $^1/_3$ seiner Fälle.

Tab. II. Durchschnittliches Erkrankungsalter in den Geburtsdezennien von 1830–1949

Geburtszeitraum	Zahl der Fälle	Durchschnittliches Erkrankungsalter	Standard-abweichung	Vertrauensgrenzen für den Mittelwert bei Rückschluß-wahrscheinlichkeit von 95%
1830–1839	15	43,33	12,5	36,43–50,23
1840–1849	22	45,45	13,2	39,59–51,32
1850–1859	31	47,07	12,3	42,57–51,56
1860–1869	79	45,46	11,4	42,90–48,01
1870–1879	157	44,87	11,6	43,04–46,70
1880–1889	251	45,12	11,5	43,69–46,55
1890–1899	354	42,75	10,0	41,70–43,81
1900–1909	368	36,61	8,6	35,72–37,50
1910–1919	129	31,28	7,4	29,99–32,57
1920–1929	52	24,12	5,7	22,54–25,69
1930–1939	12	16,00	4,6	13,05–18,95
1940–1949	3	10,67	3,1	3,07–18,26
1830–1949	1 473	40,18	11,7	39,58–40,78

Bei dem oben aus unserem Gesamtmaterial errechneten durchschnittlichen Erkrankungsalter von 40.2 Jahren kann es sich aber – ebenso wie bei den Werten der Tabelle I – nicht um dasjenige Alter handeln, in dem durchschnittlich die Chorea Huntington ausbricht. Dies wird deutlich, wenn man das Material nach Geburtsjahrgängen ordnet (Abb. 1 und Tab. II). Es zeigt sich, daß ab 1900, angedeutet schon ab 1890, das durchschnittliche Erkrankungsalter laufend abnimmt, während es vorher kon-

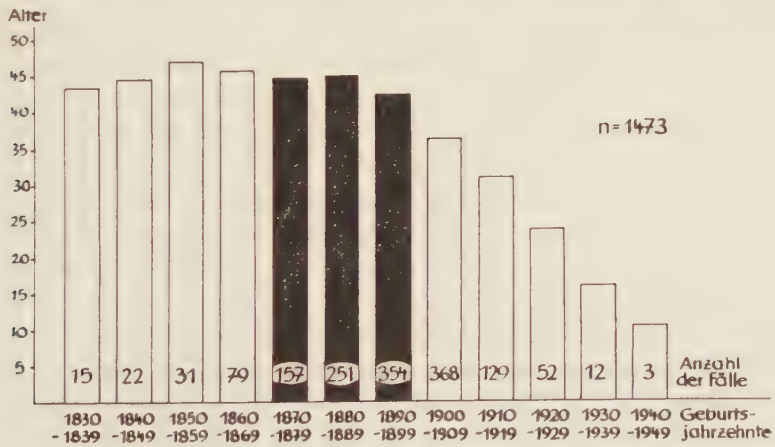


Abb. 1. Durchschnittliches Erkrankungsalter der 1830 bis 1949 geborenen Choreatiker (geordnet nach Geburtsjahrzehnten).

stant bleibt. Standardabweichung und Vertrauensgrenzen (Tab. II) zeigen an, daß dieser Rückgang des Durchschnittswertes nicht zufällig sein kann.

Berücksichtigen wir also alle Fälle unseres Materials, so enthält dies zu viel früh erkrankte Choreatiker aus den letzten Jahrzehnten, aus denen die späterkrankenden heute noch gesund und deshalb nicht erfaßt sind.

Denkbar wäre, daß der durch die Einbeziehung der Frühfälle aus den letzten Jahrzehnten entstehende Fehler dadurch ausgeglichen wird, daß aus den älteren Geburtsjahrzehnten Spätfälle häufiger registriert wurden als Frühfälle. Dann müßte der Durchschnittswert für das Erkrankungsalter am Anfang des Erfassungszeitraumes hoch liegen und langsam zu mittlerer Höhe abfallen. Von dieser mittleren Höhe müßte dann der weitere Abfall des Durchschnittswertes in den jüngsten Geburtsjahrgängen erfolgen. Dies aber ist, wie ein Blick auf Abb. 1 zeigt, an unserem Material wahrscheinlich nicht der Fall. Aber auch für den Fall, daß sich in unserer Kurve des Erkrankungsalters die fehlerhaften Abweichungen am Anfang und am Ende durch entgegengesetzte Richtung aufheben würden, fiele dennoch der durchschnittliche Wert des Erkrankungsalters zu niedrig aus. Denn der Anteil der Choreatiker, die zwischen 1900 und 1940 geboren sind, macht $^1/_3$ unseres Gesamtmaterials aus. Die Fälle zwischen 1820 und 1869 stellen dagegen nur etwa $^1/_{10}$.

Auch im Material der übrigen in Tab. I zitierten Autoren scheint uns der durch die Einbeziehung jüngerer Jahrgänge entstandene Fehler nicht durch einen entgegengesetzten Fehler bei den ältesten Jahrgängen ausgeglichen zu werden. Bei *Panse* z. B. machen die jüngeren, noch nicht abgeschlossenen Jahrgänge, $^2/_3$ seines Gesamtmaterials aus.

Den annähernd richtigen Wert für das mittlere Erkrankungsalter bei der Chorea Huntington würde man durch die vollständige Erfassung aller Krankheitsfälle aus einem bestimmten abgeschlossenen Geburtszeitraum erhalten.

Nun ist aber das Erkrankungsalter auf praktisch alle Altersstufen verteilt. In unserem Material liegen die Extremfälle im 3. und im 79. Lebensjahr. Wollte man wirklich genau sein, dann dürften also einmal Kranke nur aus solchen Geburtsjahrgängen verwertet werden, deren jüngste Angehörige heute etwa 80 Jahre alt sind. So würde kein Spätfall der Erfassung entgehen können. Zum anderen müßten aber die verwerteten Geburtsjahrgänge so liegen, daß auch extreme Frühfälle nicht der Erfassung entgehen können. Es müßte also eine genügend große Anzahl von Geburtsjahrgängen vor 1880 vollständig erfaßt sein. Dies ist jedoch praktisch nicht erreichbar. Wir haben deshalb den weiteren Auswertungen die Geburtsjahrgänge von 1870 bis 1899 zugrunde gelegt. Für diesen Zeitraum ist einerseits die Chance, daß uns Frühfälle entgangen sind, nicht mehr

groß. Andererseits können uns auch kaum noch Spätfälle entgangen sein: Die jüngsten, 1899 geborenen, Angehörigen des berücksichtigten Geburtszeitraumes müßten immerhin schon nach dem 57. Lebensjahr erkranken, um unserer Erfassung zu entgehen.

Wir können hoffen, zu einem späteren Zeitpunkt die Choreatiker (aus dem Gebiet der Bundesrepublik) für einige Geburtsjahrzehnte vollständig erfaßt zu haben. Es wird aber wahrscheinlich nicht gelingen, für *alle* diese Fälle genügend zuverlässige Informationen über den Zeitpunkt des Auftretens der ersten Krankheitssymptome zu erlangen. Daher wird es auch dann nicht möglich sein, *alle* Fälle eines bestimmten Geburtszeitraumes für die Berechnung des durchschnittlichen Erkrankungsalters heranzuziehen. Der Fehler aber, der dadurch entsteht, daß wir nur einen Teil der Fälle aus dem berücksichtigten Geburtszeitraum verwerten, wird aller Voraussicht nach nicht groß sein, da die Auswahl als zufällig und damit repräsentativ angesehen werden kann.

Berechnen wir nun für die 762 Krankheitsfälle der Geburtsjahre 1870 bis 1899 das durchschnittliche Erkrankungsalter, so ergibt sich der Wert von 43,97 Jahren (Tab. III).

Für das männliche Geschlecht ($n = 377$) allein beträgt der Durchschnitt 44,25 Jahre, für das weibliche Geschlecht ($n = 385$) wurde er mit 43,69 Jahren festgelegt. Der Geschlechtsunterschied ist nicht signifikant (Tabelle III).

Die Verteilung des Erkrankungsalters zeigt Abb. 2. Da der Geschlechtsunterschied in der Verteilung ebenfalls nur geringfügig ist, kann die nähere Betrachtung sich auf die Zusammenfassung beider Geschlechter beschränken. Der Abb. 2 ist zu entnehmen, daß 36 Prozent aller Choreatiker zwischen dem 40. und 50. Lebensjahr (genau: vom Anfang des 41. bis zum Ende des

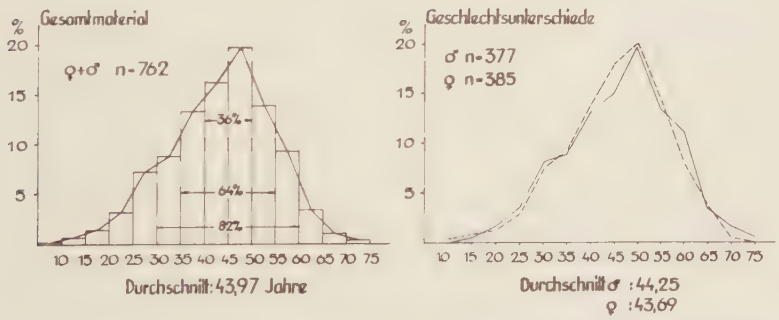


Abb. 2. Verteilung des Erkrankungsalters der Geburtsjahrgänge 1870 bis 1899 auf Lebensjahrfünfte.

Tab. III. Verteilung des Erkrankungsalters

Eigenes Material aus den Geburtsjahrgängen 1870–1899 und Material Panse

Erkrankungsalter Jahre	Häufigkeit des Krankheitsausbruches							
	Eigenes Material						Material Panse	
	♂ absolut	%	♀ absolut	%	♂+♀ absolut	%	♂+♀ absolut	%
1– 5	—	—	—	—	—	—	2	0,4
6–10	—	—	1	0,3	1	0,1	6	1,3
11–15	2	0,5	3	0,8	5	0,7	9	2,0
16–20	6	1,6	5	1,3	11	1,4	16	3,5
21–25	13	3,5	11	2,9	24	3,2	49	10,7
26–30	30	8,0	28	7,3	58	7,6	66	14,4
31–35	33	8,8	35	9,1	68	8,9	61	13,3
36–40	49	13,0	53	13,8	102	13,4	84	18,3
41–45	56	14,9	69	17,9	125	16,4	72	15,7
46–50	74	19,6	77	20,0	151	19,8	41	8,9
51–55	51	13,5	56	14,5	107	14,0	25	5,5
56–60	42	11,1	31	8,0	73	9,6	13	2,8
61–65	13	3,4	14	3,6	27	3,5	11	2,4
66–70	6	1,6	2	0,5	8	1,1	2	0,4
71–75	2	0,5	—	—	2	0,3	2	0,4
Gesamt	377	100	385	100	762	100	459	100
Durchschnitt	44,25		43,69		43,97		36,67	
Varianz	125,842		111,751		118,653		146,448	
Standartabweichung	11,2		10,6		10,9		12,1	
Vertrauensgrenzen des Mittelwertes für Rückschlußwahrscheinlichkeit von 99%	42,74 45,76		42,28 45,10		42,93 45,00		35,19 38,15	
Vergleich der Durchschnittswerte t = Test	t = 0,7074 kein signifikanter Unterschied				t = 10,8736 Der Unterschied ist mit einer I. W. von weniger als 10^{-10} signifikant			

Die statistische Bearbeitung erfolgte auf Grund der Originalwerte für die einzelnen Jahre.

50. Lebensjahres) erkranken. 64 Prozent erkranken zwischen 35 und 55 Jahren, 82 Prozent schließlich zwischen 30 und 60 Jahren. Vor dem 21. Lebensjahr bricht die Krankheit bei 3 Prozent und nach dem 70. Lebensjahr bei 1,2 Prozent aus.

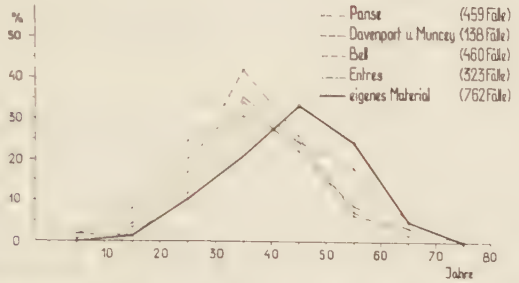


Abb. 3. Vergleich der Verteilung des Erkrankungsalters (in 10-Jahres-Gruppen) aus dem Material verschiedener Untersucher.

Die Angaben über das Ausmaß der Gefährdung in den einzelnen Lebensabschnitten sind klinisch besonders bedeutsam. Es muß deshalb geprüft werden, ob unsere Werte von denen früherer Untersucher signifikant verschieden sind. Nun ist ein Vergleich zwischen den einzelnen Autoren hinsichtlich der Verteilung des Erkrankungsalters schwierig, da die Werte teilweise nur für 10-Jahres-Gruppen mitgeteilt werden, und da zum anderen die Begrenzung der 5-Jahres-Gruppen unterschiedlich gewählt wurde. Für einen groben graphischen Vergleich mag aber eine Zusammenstellung der Verteilung in Gruppen von 10 Jahren ohne Rücksicht auf die unterschiedlichen Klassengrenzen ausreichen. Dies ist in Abb. 3 geschehen. Die Rechtsverschiebung der von uns aus geeignetem Material gewonnenen Kurve gegenüber den Kurven, die sich aus dem Material der früheren Untersucher ergeben, läßt schon vermuten, daß die einzelnen «Gefährdungszonen» für den Ausbruch der Chorea gegenüber der bisherigen Auffassung in ein höheres Lebensalter verschoben werden müssen.

Ein exakter Vergleich der von uns gefundenen Verteilung des Erkrankungsalters sei mit der Verteilung im Material von *Panse* angestellt. *Panse* gibt (in seiner Tab. 14) die Originalzahlen, die wir in 5-Jahres-Gruppen entsprechend unserer Einteilung gliedern konnten.

Auf den Vergleich mit den Ergebnissen von *Reed* wurde verzichtet, da *Reed* nicht das Erkrankungsalter, sondern den Beginn der choreatischen Unruhe bestimmt hat.

Entres hat teilweise, *Bell* ausschließlich Fälle aus der Literatur verwendet. Für beide Arbeiten ist also eine Auslese des Materials zu vermuten.

(Es werden z.B. sehr wahrscheinlich relativ zu viele Fälle mit extremem Krankheitsbeginn publiziert.) Daher hat ein Vergleich auch mit dem Material von *Entres* und *Bell* keinen Sinn. Bei den restlichen Autoren (der Tab. I) ist das Material entweder zu klein oder nicht in vergleichbarer Form mitgeteilt. Die Originalwerte (in 5-Jahres-Gruppen) für den Vergleich der Verteilung des Erkrankungsalters im Material von *Panse* mit der des eigenen Materials gibt Tab. III.

Vergleicht man zunächst die Durchschnittswerte, so findet man bei einem $t = 10{,}8736$, daß mit einer I. W. von weit weniger als 10^{-10} der Unterschied zwischen beiden Werten nicht zufällig sein kann. Beide Verteilungen wurden auch in das Wahrscheinlichkeitsnetz eingetragen. Dabei ergab sich sowohl für die Verteilung bei *Panse* wie auch für die im eigenen Material ein annähernd gradliniger Verlauf. Es besteht also keine erhebliche Abweichung von der Normalverteilung. Gleiche Steilheit beider Kurven im Wahrscheinlichkeitsnetz zeigt dazu die gleiche Varianz, die Parallelverschiebung zeigt den echten Unterschied im Durchschnittswert.

Sodann wurde geprüft, ob im Material von *Panse* und im eigenen Material die Anzahl der Erkrankungen unter 40 Jahren und über 40 Jahren eine gleiche relative Häufigkeit besitzen. Die Prüfung erfolgte mit der χ^2-Methode anhand der folgenden Vier-Felder-Tafel:

Erkrankungsalter	bis 40	nach 40	
Panse	293	266	459
Wendt	269	493	762
	562	659	

Es ergab sich ein $\chi^2_{(\mu=1)}$ von 94.49. Somit ist die sachliche Verschiedenheit beider Verteilungen mit einer I. W. von weniger als 10^{-10} gesichert.

Durch die Feststellung, daß hinsichtlich der Verteilung des Erkrankungsalters zwischen dem Material von *Panse* und den eigenen Ergebnissen ein echter Unterschied besteht, wird die – nach dem graphischen Vergleich angestellte – Vermutung bestätigt, daß die «Gefährdungszonen» für den Ausbruch einer Chorea gegenüber der bisherigen Auffassung in ein höheres Lebensalter verschoben werden müssen. Dabei ist es gleich, in welchem Umfang man diese Gefährdungszonen ansetzt.

Wenn *Panse* zum Beispiel das Hauptgefährdungsalter bei der Huntingtonschen Chorea mit der Zeit vom Beginn des 26. bis zum Ende des 45. Lebensjahres angibt und 61 Prozent seiner Krankheitsausbrüche in diesem Bereich findet, dann kann auf Grund des eigenen Materials dieser

Angabe nicht mehr zugestimmt werden. Das Hauptgefährdungsalter für das eigene Material kann etwa vom Beginn des 36. bis zum Ende des 55. Lebensjahres angesetzt werden. In diesem Bereich finden wir 64 Prozent unserer Fälle. Richtiger wäre es vielleicht noch, die Hauptgefährdungszone zwischen dem Beginn des 31. und dem Ende des 60. Lebensjahres anzusetzen. In diesem Spielraum sind dann 82 Prozent aller Erkrankungen zu suchen.

Es hat sich also gezeigt, daß die Bestimmung des Erkrankungsalters bei der Huntingtonschen Chorea an einem geeigneten Ausgangsmaterial (hinsichtlich der Erkrankungschance praktisch abgeschlossene Geburtsjahrgänge) zu einer Korrektur unserer bisherigen Vorstellungen nicht nur vom durchschnittlichen Erkrankungsalter für dieses Leiden, sondern auch von den klinisch und eugenisch wichtigen «Gefährdungszonen» für das Auftreten der Krankheit führt. Durchschnittliches Erkrankungsalter wie Gefährdungszonen liegen zweifellos höher, als bisher angenommen wurde.

Es muß aber betont werden, daß auch die an unserem Material gewonnenen Werte noch nicht völlig richtig sind. Die wichtigsten der noch nicht berücksichtigten Fehlerquellen seien noch kurz besprochen:

a) Es war schon oben erwähnt worden, daß von uns die vollständige Erfassung aller Choreatiker aus einem bestimmten Geburtszeitraum angestrebt wird, beim gegenwärtigen Stand der Erhebung jedoch noch nicht ganz erreicht ist. Falls dieses Ziel erreicht wird, spielt es keine Rolle mehr, auf welche Weise die einzelnen Fälle des Materials erfaßt wurden. Im anderen Falle aber kann der Erfassungsmodus für das Erkrankungsalter von Bedeutung sein: Wenn z. B. das Material einen merklichen Anteil solcher Kranker enthält, die nur als Eltern erkrankter Kinder erfaßt wurden, dann läge höchst wahrscheinlich der errechnete Durchschnitt für das Erkrankungsalter zu hoch: Geht man von den «Kindern» aus, haben Eltern mit vielen Kindern mehr Chancen, in das Material zu kommen als Eltern mit wenigen Kindern oder ohne Kinder. Ein Choreatiker mit *vielen* Kindern wird aber mit hoher Wahrscheinlichkeit nicht zu den früh Erkrankenden gehören. Es entsteht also durch den Erfassungsmodus sehr wahrscheinlich ein Defizit an Frühfällen. Die ausführliche Darstellung der Korrelation zwischen Erkrankungsalter und Kinderzahl soll an anderer Stelle erfolgen. Hier sei nur bemerkt, daß der durch den Erfassungsmodus mögliche Fehler für unser Material sehr klein sein muß.

b) Ein weiterer möglicher Fehler beruht ebenfalls auf der Tatsache, daß wir für die berücksichtigten Geburtsjahrgänge das Material noch nicht vollständig registriert haben. Es ist nicht sicher, ob unsere 762 Fälle wirklich eine zufällige Auswahl unter allen zwischen 1870 bis 1899 geborenen

Choreatikern darstellen. Man kann z.B. einwenden, daß für Frühfälle, besonders für solche mit kurzer Krankheitsdauer, die Erfassungswahrscheinlichkeit geringer sei. Mit dem Fortschreiten unserer Materialsammlung zur vollständigen Registrierung der Choreatiker aus den berücksichtigten Geburtsjahrgängen hin wird aber dieser Fehler immer geringer werden.

c) Eine weitere Fehlerquelle beruht auf der Tatsache, daß natürlich einige Gen-Träger *vor* Ausbruch der Krankheit sterben. Unter diesen aber müssen Spätmanifestationen relativ häufiger sein als Frühfälle. Dieser Fehler ist jedoch nicht erheblich. Da zudem klinisch nur das durchschnittliche Erkrankungsalter der wirklich Erkrankenden interessant ist, haben wir die erwähnte Fehlerquelle hier vernachlässigt.

d) Ganz allgemein entsteht bei der Bestimmung des durchschnittlichen Erkrankungsalters ein Fehler, wenn man die verwerteten Fälle aus einem bestimmten Erhebungszeitraum (und nicht aus einem bestimmten Geburtenzeitraum) heranzieht. Bei derartiger Erfassung haben Choreafälle mit langer Krankheitsdauer mehr Chancen, registriert zu werden als Fälle mit kurzer Krankheitsdauer. Frühfälle haben aber durchschnittlich eine längere Krankheitsdauer als Spätfälle.[1] Der Anteil erfaßter Frühfälle ist also dann zu groß. Dieser Fehler wird sich auch im Material von *Reed* auswirken, der von den an einem Stichtag lebenden Choreatikern ausgeht. Das betont *Reed* auch selbst.

Abschliessend sei noch bemerkt, daß die hier für die Berechnung des Erkrankungsalters bei der Huntingtonschen Chorea aufgezeigten Fehlerquellen auch allgemeine Bedeutung für die Berechnung des Erkrankungsalters bei anderen Krankheiten haben müssen.

Herrn Dozent Dr. *Vogel* (Berlin-Dahlem) sind wir für die Diskussion einiger der hier erörterten Probleme und Herrn Prof. Dr. *Heite* (Marburg) für Hinweise zur statistischen Bearbeitung zu Dank verpflichtet.

Zusammenfassung

In der bisher üblichen Berechnung des durchschnittlichen Erkrankungsalters für die Huntingtonsche Chorea steckt ein wesentlicher methodischer

[1] Diese Behauptung leuchtet ein, wenn man bedenkt, daß spät Erkrankende wegen ihres höheren Lebensalters ohnehin nur eine relativ geringe Lebenserwartung haben. Stellt man die Abhängigkeit der Krankheitsdauer (Ordinate) vom Krankheitsbeginn (Abszisse) als Punktwolke dar, so zeigt deren Ausdehnung deutlich, daß zu einem früheren Erkrankungsalter im allgemeinen eine längere Krankheitsdauer gehört. Diese Aussage wurde auch mit der χ^2-Methode gesichert. Ausführliche Darstellung dieser Abhängigkeit erfolgt an anderer Stelle.

Fehler: Die Einbeziehung der dem Erfassungszeitpunkt nahe gelegenen Geburtsjahrgänge führt zu einer Herabsetzung des wahren Durchschnittes, da aus solchen Jahrgängen zwar schon die früh erkrankten, aber noch nicht die spät erkrankenden Choreatiker erfaßt werden können.

Die annähernd richtigen Werte für den Durchschnitt und die Verteilung des Erkrankungsalters würde man an einem Material gewinnen, das auf der vollständigen Erfassung aller Choreatiker eines bestimmten Geburtszeitraumes beruht.

Die eigene Berechnung verwendet (aus den Geburtsjahrgängen 1870 bis 1899) 762 Choreatiker (377 ♂ und 385 ♀), die für verläßliche Informationen über den Krankheitsbeginn vorliegen. Es ergab sich ein durchschnittliches Erkrankungsalter von 44 Jahren. Ein signifikanter Geschlechtsunterschied besteht nicht. 36 Prozent der Choreatiker erkranken zwischen 40 und 50 Jahren, 63 Prozent zwischen 35 und 55 und 82 Prozent zwischen 30 und 60 Jahren. Beim statistischen Vergleich mit dem Material von *Panse* zeigt sich, daß Durchschnittswert und Verteilung durch die Berücksichtigung der genannten Fehlerquelle signifikant in ein höheres Lebensalter verschoben sind. Somit werden auch die klinisch und eugenisch bedeutsamen Gefährdungszonen für den Ausbruch einer Chorea später angesetzt werden müssen als bisher.

Die genaue Bestimmung des durchschnittlichen Erkrankungsalters ist bei näherer Betrachtung eine höchst schwierige und komplizierte Aufgabe. Auch die hier vorgelegten Ergebnisse sind noch nicht völlig fehlerfrei. Weitere Fehlerquellen werden diskutiert.

Summary

The author discusses some of the sources of bias and error in evaluating the mean age at onset of a disease in connection with a study of Huntington's Chorea. As stressed by the author an essential error is introduced if individuals born in the later part of the period preceding the time of investigation are taken into consideration, as only patients with an early onset of the disease can be included from this period. This naturally causes a decrease in the mean age.

To date, the author is working on a survey of all cases of Huntington's Chorea ever observed in Western Germany since the middle of the last century.

In order to obtain a more correct estimate of the age of onset the author has used 762 cases born in the period 1870–1899, where valid information as to the age of the patient at the onset of the symptoms could be obtained.

The resulting estimate of the mean and the distribution of the age at manifestation is significantly higher than those found previously.

Résumé

Les auteurs, en prenant comme exemple la chorée de Huntington, discutent quelques sources de biais et d'erreurs qui se produisent lors de l'évaluation de l'âge moyen de la manifestation d'une affection. Ils relèvent notamment qu'une erreur essentielle est introduite, si des individus nés dans la dernière partie de la période précédant l'époque de l'investigation sont pris en considération, puisque seulement des malades avec une manifestation précoce de l'affection peuvent être retenus de cette période. Ce mode d'évaluation conduit naturellement à une diminution de l'âge moyen du début de l'affection.

Les auteurs entreprennent actuellement une enquête sur tous les cas de chorée de Huntington qui ont été observés en Allemagne occidentale depuis le milieu du siècle passé.

Pour procéder à une estimation plus correcte de l'âge de la manifestation, les auteurs ont utilisé 762 cas nés dans la période de 1870 à 1899, pour lesquels ils ont pu obtenir des informations précises quant à l'âge du malade lors des premiers symptômes. L'estimation de la moyenne et la distribution de l'âge de la manifestation sont significativement plus élevées que celles trouvées auparavant.

LITERATUR

Bell, J.: Nervous diseases and muscular dystrophies, Part I: Huntington's Chorea in: The treasury of human inheritance, (Vol. IV, Cambridge University Press, Cambridge 1934).

Davenport, C. B. and E. B. Muncey: Huntington's chorea in relation to heredity and eugenics. Amer. J. Insan. *73:* 195–222 (1916).

Entres, J. L.: Zur Klinik und Vererbung der Huntingtonschen Chorea in: Monogr., Neurol. Psychiat. H. *25* (1921).

Hughes, E. M.: Social significance of Huntington's chorea. Amer. J. Psychiatr. *4:* 537–574 (1925).

Panse, F.: Die Erbchorea, in: Sammlung psychiatr. und neurolog. Einzeldarstellung, Vol. XVIII (Thieme, Leipzig 1942).

Reed, T. E. and *J. H. Chandler:* Huntington's chorea in Michigan. Amer. J. hum. Genet. *10:* 201–225 (1958).

Sjögren, T.: Vererbungsmedizinische Untersuchungen über Huntingtons Chorea in einer schwedischen Bauernpopulation. Z. menschl. Vererb., KonstitLehre *19:* 131–165 (1936).

Adresse des Autors: Dozent Dr. med. G. G. Wendt, Diätendozentur für Anthropologie am Anatomischen Institut der Universität *Marburg* (Lahn)

Freire-Maia, N.; Quelce-Salgado A. and *Amundsen Koehler, R.*: Acta genet. 9 : 33—40 (1959)

From the Laboratory of Genetics, Faculty of Philosophy, University of Paraná, Curitiba, Pr., Brazil

HEREDITARY BONE APLASIAS AND HYPOPLASIAS OF THE UPPER EXTREMITIES[1]

By N. FREIRE-MAIA, A. QUELCE-SALGADO and R. AMUNDSEN KOEHLER

Introduction

Congenital amputations and related aplasias and hypoplasias of bone have been relatively poorly studied from the genetic viewpoint. With the exception of the excellent monograph by *Birch-Jensen* (1949) and a few other papers, most reports on these osteodystrophies present them either as medical curiosities or as material for prosthetic rehabilitation. The geneticist who reviews the literature on these cases will discover that this efforts will be highly unrewarding due to the almost complete absence of familial information.

These osteodystrophies appear in the literature either as sporadical cases or in pedigrees showing dominant inheritance, with penetrance varying from very low to apparently complete. Cases suggesting recessive inheritance do exist, but with the exception of achiropody (*Freire-Maia, Freire-Maia and Quelce-Salgado*, 1958, 1959), most of these cases have not been fully studied. This paper will present a second instance of apparently recessive transmission of a congenital anomaly of the bones of the upper extremities.

[1] This research was supported by grants from the National Research Council of Brazil, the Rockefeller Foundation and the Research Council of the University of Paraná.

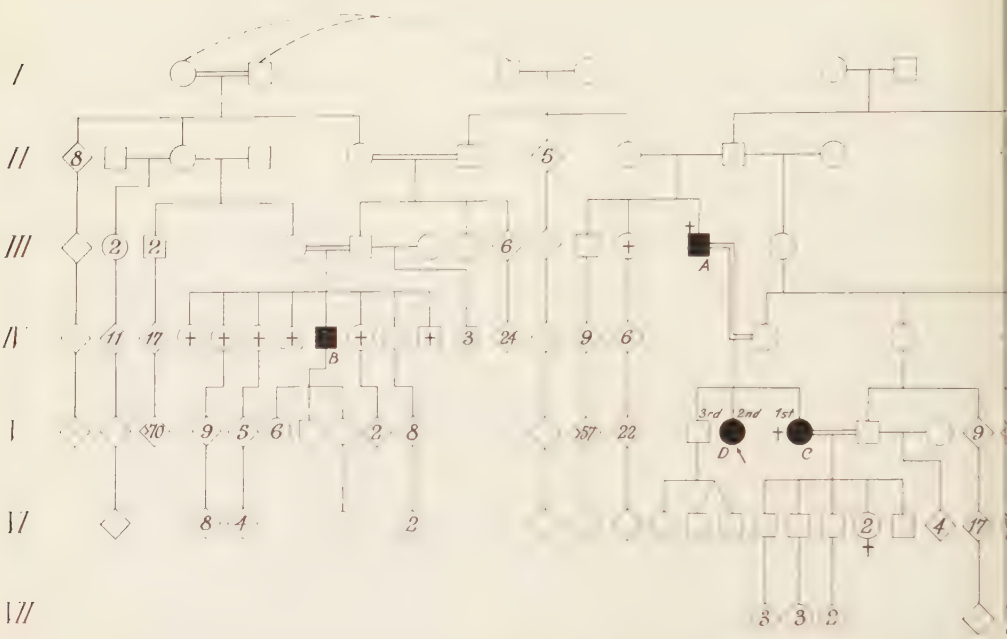


Fig. 1. An abridged pedigree of the family reported in the text. With the exception of the sibship which includes two defective individuals, the birth orders of individuals in other sibships are equal to the position of the symbols reading from left to right. Diamonds (males and females) without numbers represent sibships of unknown size. The dotted lines on the left upper part of the pedigree represent consanguinity of unknown degree. Death (†) is only reported in the sibships with at least one abnormal individual. One of the six unmarried daughters of IV–B is dead. The arrow indicates the propositus.

Fig. 2. Individual III-A.

Fig. 3. Individual IV–B.

Data

Fig. 1 presents an abridged pedigree of a Brazilian family of Portuguese ancestry, in which four amputees have been born. The pedigree encompasses 540 individuals (244 females, 223 males and 73 of unknown sex) and 158 marriages. Of the latter, 19 (i.e. 12.03%) are consanguineous (4 with unknown degrees of consanguinity). Coefficients of inbreeding (f) for the consanguineous marriages vary from 0.015625 to 0.125; the mean coefficient of inbreeding for all marriages is 0.0072 (the unknown values of f are taken to be 0).

The principal bony findings on the four amputees are as follows:

1. III–A: This patient who died at the age of about 50 was not seen by the authors; however from inspection of a photograph (Fig. 2) and information received from several of his relatives (including his daughter V–D), he had complete absence of the left upper extremity and only two fingers on the right.

Fig. 4. Radiograph of the right forearm and hand of individual IV–B.

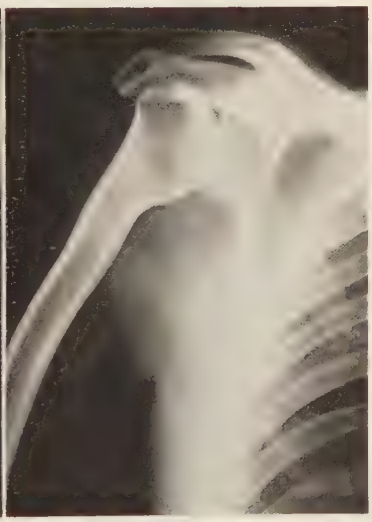


Fig. 5. Radiograph of the right scapular region of individual IV–B.

2. IV–B (fig. 3): A 43-year-old, white male exhibits, on the right, a modification of the configuration of the articular elements of the shoulder and elbow, bowed humerus, typical aplasia of radius with all the associated defects such as a short, thick and bent ulna, absence of 5 carpal bones

Fig. 6. Radiograph of the left scapular region of individual IV–B.

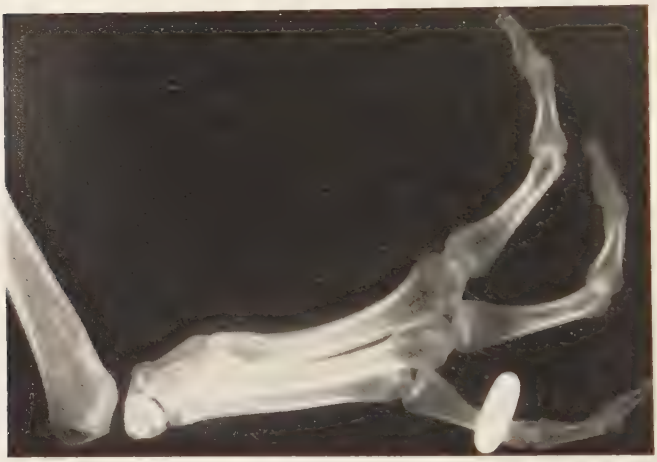


Fig. 7. Left forearm and hand of individual IV–B.

and first radial ray and manus vara (cf. also figs. 4 and 5). On the left (cf. figs. 6 and 7), there is an hypoplasia of the humerus, whose remaining part (with rather irregular countours) is disarticulated from the glenoid fossa, an aplasia of the radius, bowed ulna, absence of some carpal bones, absence of first and second radial rays, and manus vara.

3. V–C: This patient who died at the age of about 40 was also not seen by the authors. She had pronounced bilateral peromelia, the details of which could not be ascertained with accuracy. From fig. 8, however, one can establish an absence of some radial rays, manus vara, and a prob-

Fig. 8. Individual V–C.

Fig. 9. Individual V–D.

able hypoplasia of the humerus. This case is in many respects similar to patient IV–B (cf. fig. 3). Information received from relatives as well as the analysis of another photograph revealed that V–C had only three fingers on each hand (with partial syndactyly on the left) and that her right arm was about twice the length of her left arm.

4. V–D (propositus, figs. 9 and 10): A 53 year old, white female with hypoplasia of both clavicles and scapulas, and absence of the glenoid fossae. On the left, there is an aplasia of the whole upper extremity and the presence of a rounded prominence constituted of soft tissues. The right

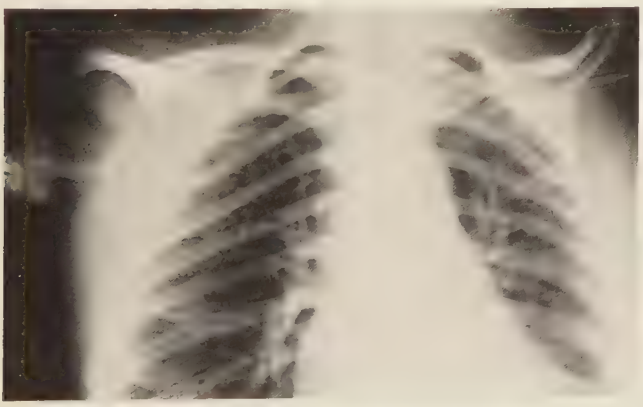


Fig. 10. Radiograph from individual V–D.

upper extremity consists of only one finger with only two phalanges and five other bones without precise roentgoenological characteristics but which could be interpreted as one metacarpal, two carpals, radius and humerus, the two latter highly hypoplastic.

Discussion

The presence of four congenital amputees in the same kindred is a clear suggestion of a genetic component in the etiology of the malformation. In the present instance while each case is, in many respects, unique they are similar in exhibiting more pronounced changes on the left than on the right side. The four can be grouped into two pairs on the basis of the degree of similarity in their defects (III–A and V–D; IV–B and V–C).

For genetic analysis, the following eight observations are pertinent:

1. Two of the three marriages giving rise to defectives are consanguineous (first cousins and uncle × half niece).

2. The anomaly affects both men and women (2:2).

3. The ratio of 9 normals to 2 abnormals in the pooled data from sibships derived from normal parents approximates the 3:1 ratio expected of simple recessive heredity. Among the offspring of individual III–A, where a ratio of 1:1 would be expected on the assumption of an autosomal recessive gene, are two abnormal children and one normal.

4. Two of the abnormal individuals (IV–B and V–C) have had a total of 14 normal children and no abnormal ones. The only amputee (III–A) who has produced defective children was married to a half niece.

5. Two of the four amputees (III–A and IV–B) are children of normal parents. The two exceptions (referred to in the last paragraph) are the offspring of a consanguineous marriage.

6. As two of the defective individuals (V–C and V–D) are the first and second born in a sibship of three, the third (III–A) is the third born in a sibship of three, and the fourth individual (IV–B) is the fifth born in a sibship of eight (the pooled data showing the abnormals as first, second, third and fifth born), there is no reason to suspect a correlation between birth rank and the appearance of the trait.

7. The viability of the abnormal individuals does not seem to be lower than that of their normal relatives. All of the defective persons reached adulthood. Individual III–A died at about 50 years of age from tetanus and V–C died at approximately 40 years of age from a heart attack.

8. The fertility of the malformed members of this kindred does not seem lower than that of their normal siblings. Three of them (III–A, IV–B and

V-C) have married and had a total of 17 children (11 females and 6 males). The mean number of children per defective is 4.25 while the comparable figure for their normal siblings is 4.20 (42 10). If one uses only the individuals with at least one child, the respective figures turn out to be 5.67 ± 1.19 and 6.00 ± 0.99. From these data, there is no reason to believe that the disfiguring nature of the anomaly has an effect either on the frequency of marriage or reproduction. It is important to point out, however, that this conjecture is valid only for the particular region and social level from which the defectives are drawn. This family is from a low social stratum in South rural Brazil. It is probable that in a more sophisticated society the same anomaly would be highly selected against if only for cosmetic reasons. It is interesting to compare this situation with that found for achiropody, a much more disfiguring anomaly (cf. *Freire-Maia, Freire-Maia and Quelce-Salgado*, 1958, 1959). In the latter instance, the net fertility of the trait bearers is affected by socio-psychological and survival factors (for an analysis of the basic components of net fertility, see *Crowe, Schull and Neel*, 1956).

Conclusions: I. Points 1 to 6 in the above suggest the action of an autosomal recessive gene (with variable expressivity). II. Points 7 and 8 indicate that this gene does not seem to be under the action of strong selective forces in the particular pedigree analysed.

ACKNOWLEDGMENTS

We are indebted to several members of this family, especially to Miss *Mariana Machado* and Mr. *Joaquim Machado Bonfim*, for their understanding and help. Our thanks are also due to Dr. *William J. Schull* for reading and criticizing the manuscript.

Summary

A pedigree with four cases of peromelia involving the upper extremities is presented. The data suggest the action of an autosomal recessive gene with variable expressivity. Fertility of the trait bearers does not appear to be impaired. The action of natural selection on disfiguring anomalies in man is briefly discussed.

Zusammenfassung

Es wird ein Stammbaum mit 4 Fällen von Peromelie an den oberen Extremitäten dargestellt. Die Angaben lassen auf ein autosomal-rezessives

Gen mit variabler Expressivität schließen. Die Fruchtbarkeit der Merkmalsträger scheint nicht beeinträchtigt zu sein. Die Wirkung der natürlichen Auslese auf entstellende Anomalien beim Menschen wird kurz besprochen.

Résumé

Un arbre généalogique avec quatre cas de péromélie des membres supérieurs est décrit. Les résultats suggèrent l'action d'un gène récessif autosomique avec expressivité variable. La fertilité des porteurs de l'anomalie ne semble pas réduite. Les auteurs discutent brièvement l'effet de la sélection naturelle dans le cas d'anomalies défigurantes.

REFERENCES

Birch-Jensen, A.: Congenital deformities of the upper extremities. Opera Ex Domo Biol. Hered. Hum. Univ. Hafn., vol. 19 (Ejnar Munksgaard, Copenhagen 1949).

Crowe, F. W.; Schull, W. J. and *Neel, J. V.:* A clinical, pathological and genetic study of multiple neurofibromatosis; 182 p. (Charles C. Thomas, Springfield. Ill. 1956).

Freire-Maia, A.; Freire-Maia, N. and Quelce-Salgado, A.: Genetic aspects of achiropody. Proc. 10th int. Congr. Genetics, Montreal, pp. 88–89 (Univ. of Toronto Press, 1958).

Freire-Maia, A.; Freire-Maia N. and Quelce-Salgado, A.: The achiropody gene. Proc. 1st brazil. Meeting human. Genet. (1959a, in press).

Freire-Maia, N.; Freire-Maia, A. and Quelce-Salgado, A.: Methods of ascertainment and analysis in medical genetics with special reference to the problem of congenital amputations. Proc. 1st brazil. Meeting hum. Genet. (1959b, in press).

Authors' Address: Dr. N. Freire-Maia, A. Quelce-Salgado and R. Amundsen Koehler, Laboratory of Genetics, Faculty of Philosophy, University of Paraná, *Curitiba*, Paraná (Brazil).

Arnvig, J.: Acta genet. 9 : 41—46 (1959)

From the Department of Otolaryngology (Head: Jørgen Arnvig, M.D.),
The State Hospital, Sønderborg, Denmark

THE SYNDROME OF WAARDENBURG

By JØRGEN ARNVIG

In 1950 the Dutch ophthalmologist *Waardenburg* presented a syndrome of inherited anomalies comprising a hyperplasia of the interocular region, certain disturbances of pigmentation, and deafness of one or both ears. Most of these genetic traits were inherited dominantly, the ear-disease, however, was considered to be of a recessive inheritance.

Waardenburg's latest publication on this subject appeared in 1957. Moreover papers have been published in Holland by *Wildervanck* (1957), in Switzerland by *Bischler* (1955), and in England by *Fisch and Renwick* (1956). *Waardenburg* believes in a general occurrence of his syndrome, but with varying incidence.

According to the features of the phenotype, *Waardenburg* designates the disease: Hyperplasia interocularis, dyschromia iridocutanea et dysplasia auditiva. The appearance therefore is rather characteristic. The eyes are situated wide apart and, as distinct from hypertelorism, the palpebral fissures are small and the medial commissure of the eyelids conceals most of the medial sclera. The root of the nose is broad and being lofty and powerful it often gives the profile a Grecian character.

The anomalies of pigmentation generally appear to a varying extent and sometimes they are missing. Mono- or bilateral heterochromia of the iris is a common trait, as well as discoloration of a hairlock or an eyebrow. Early grayness of the hair is rather common too, for instance beginning soon after the age of puberty. Defective pigmentation may occur elsewhere on the body.

Waardenburg does not believe in a linkage of the genes. He interpretes the phenomenon as a polyphenous characteristic, because deafness in asso-

ciation with bilateral hypochromia or with heterochromia is met with in animals, and due to the fact that either the white hairlock or the irishypochromia or the deafness may prevail in some of the families suffering from the syndrome. Further supporting evidence is given by the distribution of the individual symptoms which may be quite irregular within the same family along with a distinct monogenous nearly regular dominance of the symptoms concerning the eyelids and the root of the nose.

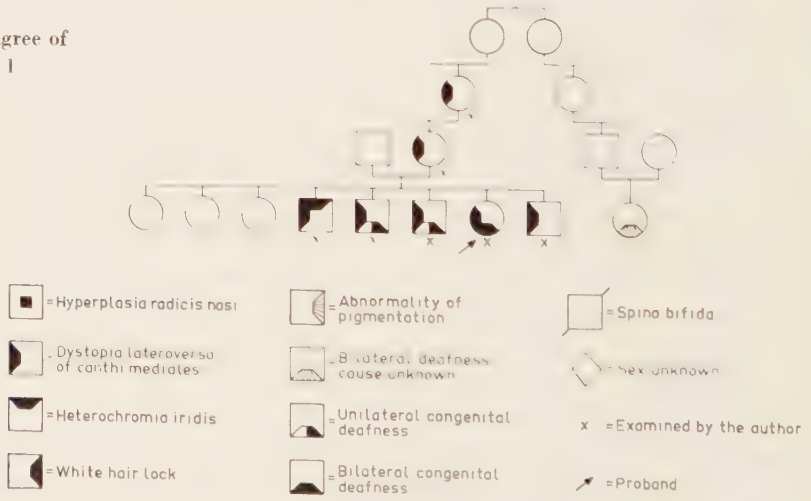
The mono- or bilateral hearing impairment is usually severe. Occasionally – as in the present series – bilateral cases are seen with normal speech owing to a more moderate affection of the one side.

The vestibular organ is often involved as is frequently the case with inherited hearing impairment.

Case records

1. Girl S.D.H., aged 14 (The State School for the Deaf, Fredericia). No. 7 of 8 siblings. Severe hardness of hearing (Audiogram 1). The features of herself (fig. 1) and her four brothers resembled those of the mother and the maternal grandmother. Two of the brothers had monolateral abolished function of the 8th nerve, the other ear being quite normal. Another brother had irisheterochromia. The maternal grandmother's cousin had a deaf-mute grandchild. (Pedigree of case 1.)

Pedigree of case 1

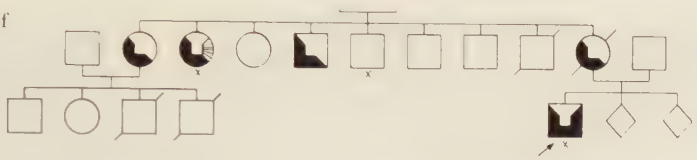


2. Man E.P., aged 29 (Home for Deaf Men, Nyborg). His features were like those of the mother and three of her brothers and sisters (fig. 2). He

had a white hairlock at the back of his head (fig. 2a). All the bearers of the deformity of the eyelids and nose had always been deaf too. One of them was white-haired about the age of 20.

Some of the family members and not only the bearers of the syndrome suffered from spina bifida. (Pedigree of case 2.)

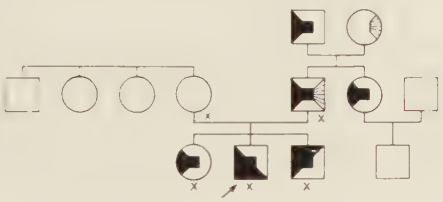
Pedigree of case 2



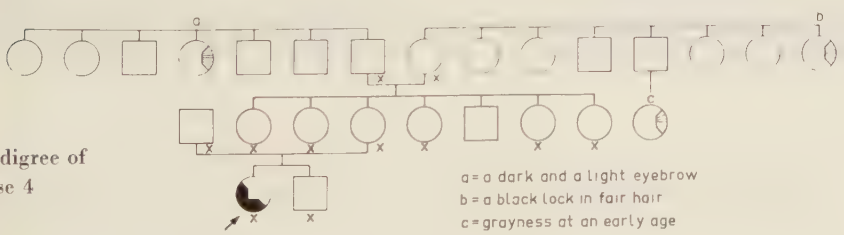
3. Boy J.K., aged 10 (The State School for the Deaf, Fredericia). No. 2 of 3 siblings (fig. 3), all having the characteristical features, quite like those of the father and the paternal grandfather. Severe hardness of hearing (Audiogram 2). This boy is the only known deaf in the family, the father, however, having no knowledge of other relatives but his parents.

The sister of the proband had a definite hyperplasia of the nose root (fig. 4), and the brother had a blue and a brown iris. The father's hair turned gray after the age of 17. (Pedigree of case 3.)

Pedigree of case 3



4. Girl D.A., aged 5 (The State Hospital, Sønderborg). No. 1 of 2 siblings. Her speech was normal. The characteristic deformity of the eyes (fig. 5) could not be traced back to any other family member. The audiogram (no. 3) revealed a severe bilateral perception loss, the frequencies below 1000 Hz being preserved on the left side.



Pedigree of case 4

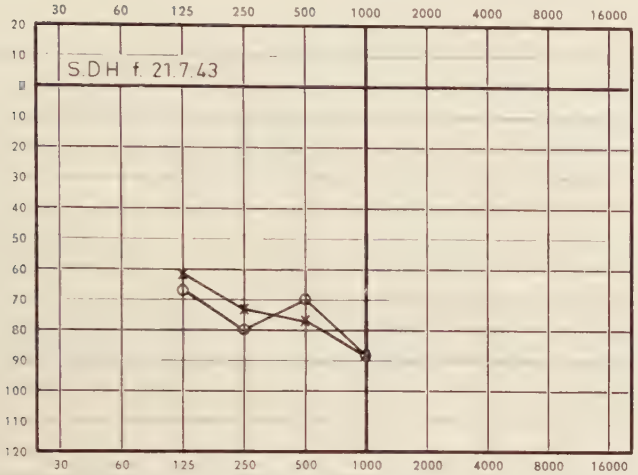
No pigmentation abnormalities could be demonstrated in the proband, but to a lesser degree these were found in some of the family members.

No hearing impairment could be demonstrated among the relatives.

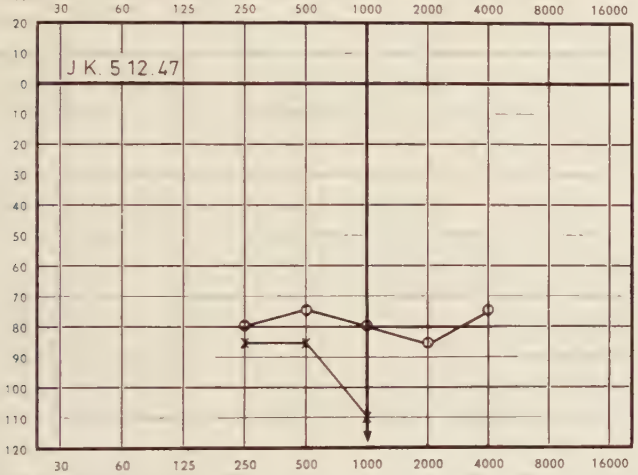
Possibly this case is due to a mutation. (Pedigree of case 4.)

Fig. 1, 2, 2a, 3, 4 and 5

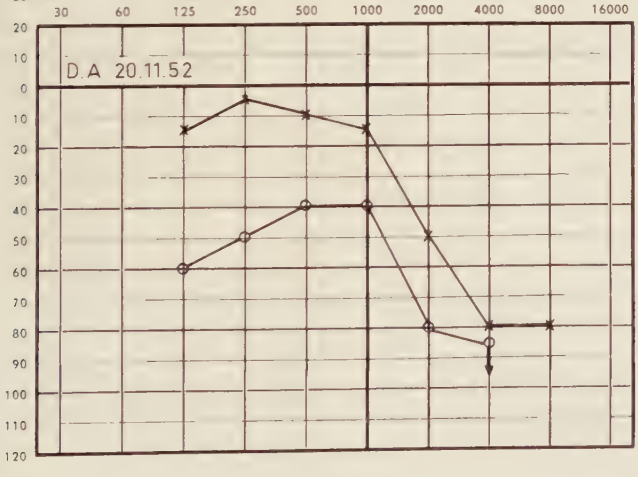
The photos illustrate the appearance of the eyes and the hyperplasia of the nose root in Waardenburg's syndrome. Fig. 2, case 2, was the only patient in the series with a white hair lock (fig. 2a). Fig. 3 and 4 are brother and sister, the latter having normal hearing.



Audiogram 1



Audiogram 2



Audiogram 3

Summary

Four cases of the syndrome of *Waardenburg* are presented. The inherited anomalies comprise a hyperplasia of the interocular region, certain disturbances of pigmentation, and mono- or bilateral deafness.

Zusammenfassung

Es werden 4 Fälle des Waardenburg-Syndroms dargestellt. Die vererbten Anomalien umfassen eine Hyperplasie der interokulären Region, gewisse Pigmentstörungen sowie ein- oder zweiseitige Taubheit.

Résumé

L'auteur décrit quatre cas de syndrome de Waardenburg. Les anomalies transmises comprennent une hyperplasie de la région inter-oculaire, des troubles de la pigmentation et une surdité uni- ou bilatérale.

REFERENCES

Bischler, V.: Rev. suisse Zool. *62:* 83 (1955) (cit. *Waardenburg*).

Fisch, L. and Renwick, T. K.: Teach. Deaf. *54:* 130 (1956) (cit. *Waardenburg*).

Waardenburg, P. J.: Hyperplasia interoculares cum dystopia lateroversa canthi medialis, blepharophimosis, dyschromia iridocutanea et dysplasia auditiva. Acta ophthal., Kbh. *35:* 311 (1957).

Wildervanck, L. S.: Doofstomme kinderen met het syndroom *van Waardenburg-Klein*. Ned. T. Genessk. *101:* 1120 (1957).

Author's address: Dr. Jørgen Arnvig, Statshospitalet, *Sønderborg* (Denmark)

Ueno, S.; Suzuki, K. and *Yamazawa, K.*: Acta genet. *8*: 47—53 (1959)

From the Department of Legal Medicine, Faculty of Medicine, University of Tokyo

HUMAN CHIMERISM IN ONE OF A PAIR OF TWINS

By SHOKICHI UENO, KAZUO SUZUKI and KICHIHEI YAMAZAWA

The condition of "chimera" (the term which has long been used in the botanical field to denote an individual plant in which there are two or more tissues differing in their genetic constitution, such as a graft hybrid) was first demonstrated in mammals by *Lillie* (1) in 1916. He explained the freemartin condition of a bovine twin sister by the existence of the union of the circulatory systems of twin embryos and the effects of hormones of the opposite sex on sex-differentiation and sexual development. The same condition will result in an interchange of erythroblasts with production throughout life of two sorts of blood of different blood groups (*Owen*, 2). Chimeras which seem not to be so rare in cattle twins, are an extraordinary occurence in a human being. The first case was reported in 1953 by *Dunsford, Boucley, Hutchison, Thompson, Sanger* and *Race* (3). The second case was that of ours (4). We found this in a applicant for the entrance examination of the Junior High School attached to the University of Tokyo in February, 1956. She was then 12 years and 6 months old and one of a pair of fraternal twins. Her twin brother, however, turned out to be normal. This is exceptional, because it is generally believed that in cases of chimeras both twins show the evidence of admixture, as we see it in cattles. From this reason this pair of twins was carefully examined for more than one year and finally the result was reported at the 41st annual meeting of the Medico-legal Society of Japan on June 21, 1957. Soon after the publication we have learned that two

more examples of human blood chimera had been reported by English investigators (*Booth. Plaut. James. Ikin. Moores. Sanger* and *Race* [5] and *Nicholas. Jenkins* and *Marsh* [6]): they both appeared in the British Medical Journal, which was issued on June 22, 1957. The paper of the present authors presents details of the experimental data of the same case, already reported, which, we believe, have some peculiar features.

Miss Y.Y. is one of a pair of twins of different sex. Her red cells appeared at first to be a weak form of group A; when mixed with anti-A or with anti-A+B on a slide and examined through the microscope very small agglutinates were seen which were outnumbered by unagglutinated cells; anti-B caused no agglutination. Her serum contained anti-B but no anti-A. Her twin brother's blood was found normal, as well as those of her parents and her elder sisters.

Separating 0 and A red cells of Miss Y.Y.

Anti-A or anti-A+B is added to the 5% red cell suspension of Miss Y.Y. in an equal amount and placed in room temperature for 30 minutes. The agglutinated A cells sank very quickly to the bottom and these were separated and freed from agglutinin by shaking and washing several times in saline (at 56°C). The remaining non-agglutinated cells were taken from the supernatant fluid and washed in saline. Blood cells thus separated were checked as to their blood groups. For this grouping the antibodies anti-A, A_1, B, A+B; anti-M, N; anti-Q; anti-C, D, E, c, e, were used, appropriate controls employed throughout. The results are shown in the Table 1.

Table 1.

Red Cells of Proposita:
Results of Blood Group Tests.

Red cells	Anti-											
	-A	-A	A B	-B	-M	-N	-Q	-C	-D	-E	-c	-e
Untreated	+++*	+++*	+++*	—	+++	+++*	—	+++	+++			+++
Separated (I)	+++	+++	+++	—	+++	—	—	+++	+++	—	—	+++
Separated (II)	—	—	—	—	+++	+++	—	+++	+++	—		+++

The asterisk means that unagglutinated cells were very obvious.

The blood cell counts were made on the total and on the non-agglutinated 0-red cells and the computation of the proportion of two kinds of red cells was done twice as shown in the following Table 2.

Table 2.
Red Cell Counts in the Proposita.

	Feb. 1956	May 1957
Total Blood (untreated)	$349 \times 10^4/mm^3$	$352 \times 10^4/mm^3$
0-separated	$239 \times 10^4/mm^3$	$245 \times 10^4/mm^3$
Ratio A:0	31.6:68.4	30.4:69.6

As the Table shows, no great change was observed after a lapse of over one year. The twin brother's blood was checked carefully and even after scrutinizing examination no abnormalities were found; it was a perfectly normal and uniform blood, and his blood group coincided exactly with the A blood of his twin sister, Miss Y.Y. The blood groups of the family are shown in the following pedigree (see Fig. 1).

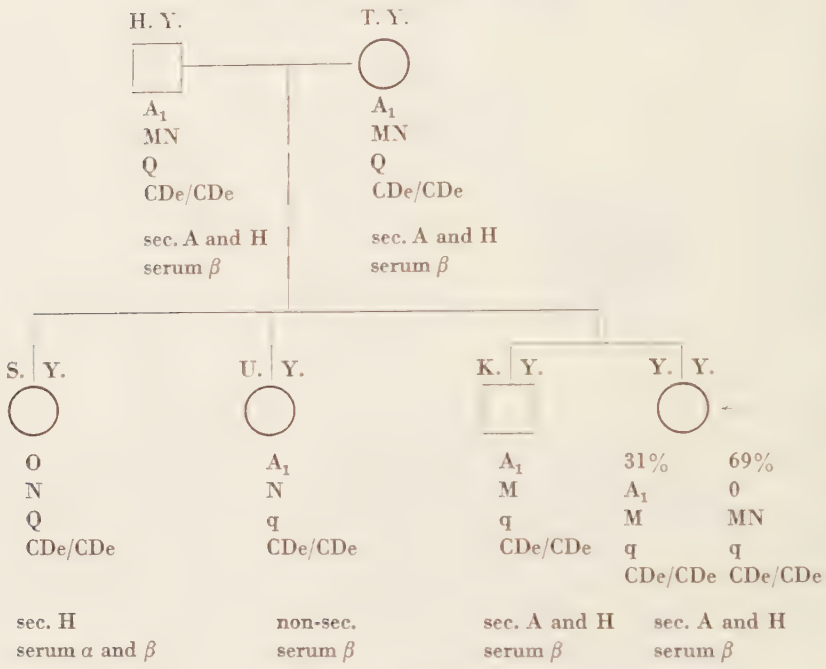
If the admixture of blood in Miss Y.Y. is the result of the so-called chimerism, the A blood is the grafted and the 0 blood the inherited. In chimerism the embryonic blood vessels from each twin are considered to anastomose in the connecting part of the chorion, so that either foetus can be injected from the other. The two cases of hitherto reported chimera twins (5, 6) were concordant as both twins contained mixtures. In our case, however, only one of them is a chimera. It is not strange if it does happen that the transplanted primordial cells from the partner takes root in only one of the twin foetus.

Secretor-types of the twins

For testing H and A substances in saliva serial doubling dilutions of saliva heated for 10 min. at 100°C were mixed with one volume of diluted anti-H and anti-A serum (containing 8 units of antibodies) and left at room temperature for 30 min. Anti-H is anti-human 0 red cell immune chicken serum and anti-A that of human origin. After incubation one drop of 2% 0 and A red cell suspension respectively was added and after another 30 min. incubation the mixture was examined by the aid of a hand lens

Fig. 1.

Pedigree of the Family of the Proposita.



Arrow = Proposita

of 8-fold magnification. The maximum dilution of the inhibition in agglutination was recorded. The results are shown in the Table 3.

Table 3.

Antigen Secretion in the Proposita and her Family.

	Twins		Twins' sister	Twins' father	Twins' mother
	Miss Y.Y. (A_1+0)	Mr. K. Y. (A_1)	Miss S. Y. (0)	Mr. H. Y. (A_1)	Mrs. T. Y. (A_1)
H	64	4	64	32	8
A	32	128	< 1	128	64
Results	sec. H+A	sec. H+A	sec. H	sec. H+A	sec. H+A

Both twins are secretors, varying, however, in the amount of each antigen secreted: the secretion of the H antigen in the saliva was far larger, of the A antigen far smaller in the proposita than in her twin brother.

It is generally known that the secretor and non-secretor differentiation can also be made by the amount of group substances contained in the body fluids, such as gastric juice, semen and urine. The urine of the twins was also the object of our examination for H and A antigens, but only after the extraction of a carbohydrate fraction.

500 ml urine were condensed to a volume of about one-fifth on the boiling water bath and then filtered. The filtrate was allowed to dialyse in a cellophane bag against running water. After dialysis it was again concentrated into 10 ml on a water bath and 80 ml 96% alcohol was added in order to precipitate the carbohydrate fraction. After a standstill in the cold for 24 hours it was centrifuged and the precipitate was dissolved in a small amount (4–5 ml) of water. After discarding the undissolved part 25 ml 96% alcohol was added to give a maximum precipitation. The precipitate was dissolved in 5 ml saline, starting from this, serial doubling dilutions were made. Further, the same procedure was followed as when saliva is examined. The results are shown in Table 4.

Table 4.

Antigen Secretion in the Urine of the Proposita and her Twin-Brother.

Group antigen	Twins		Controls	
	Miss Y.Y. (A_1+0)	Mr. K.Y. (A_1)	Mr. Okajima (0)	Mr. Takei (A_1)
H	32	16	64	4
A	64	64	<1	128
Results	sec. H+A	sec. H+A	sec. H	sec. H+A

Miss Y.Y. secretes in her urine A as well as H antigen, the latter in a little larger amount than her twin brother does.

Agglutinins in the serum

The serum of the proposita contains anti-B agglutinin with a titre of 1:32. Tests at various temperatures in saline, serumalbumin or with anti-

human globulin serum failed to demonstrate anti-A either free in the serum or blocking or coating the cells. No irregular antibodies were detected. The serum of her twin brother showed no abnormality and contained anti-B agglutinin with a titre of 1:64.

White cells of the twins

White cells contain group antigen corresponding to the blood groups of the red cells (*Kuo*, 7); the white cells of individuals belonging to group A will be agglutinated by anti-A serum. The white cells of Miss Y.Y. and also of Mr. K.Y., her twin brother, were agglutinated by anti-A almost in the same strength, but in the former a far greater number of non-agglutinated cells were seen by microscopic examination. This fact was compatible with a mixture of 0 and A white cells in Miss Y.Y.'s blood.

Discussion

We have dealed with a pair of binovular twins of different sex, only one of whom presents a mixture of 0 and A group red cells. Separation was successful by using anti-A serum but was only so in part by differential agglutination with a potent anti-N rabbit serum, probably because the latter contains some amount of heterologous agglutinins. The anomaly is considered to have arisen from so-called chimerism. The concept of somatic mutation is excluded by the occurrence of the involvement of two blood group systems – AB0 and MN.

The propositus, Miss Y.Y. secretes A as well as H antigen in her saliva and her serum contains only anti-B agglutinin. Generally speaking, the secretion of A antigen in the saliva depends on the presence in the genotype of the A gene as well as the secretor gene and without an A gene the individual can not secrete an A antigen present only in the circulation. The above-mentioned facts seem to show that her genetic group must be A and her 0 blood is transplanted from her twin brother. But this seems improbable, because her twin brother's blood group is A and does not contain 0 blood. He is also a secretor of H and A. Another possibility is, therefore, highly probable, that is, her 0 blood is inherited and her A blood is grafted from her twin brother by intrafoetal anastomosis and the chimerism in this case must have been extended to the salivary gland and other tissue cells. If a grafting of tissue cells had actually occurred, they could produce A antigen, irrespective of their having an A gene or not. A chimerism which involves tissue cells as in our case has not been reported previously.

Miss Y.Y. is feminine in appearance and her genital organs are seemingly normal, and she had already experienced her first menstruation. Whether she is a freemartin or not still remains to be decided. If she can have a child in future, her genetic group will be clearly established by examining the blood group of her offspring.

Summary

We have reported a case of human chimerism found in one of a pair of twins of different sex, the chimerism seemed to have involved the tissue cells as well as the blood cells.

We are indebted to Miss Y.Y. and all her family for their cooperation in this investigation.

Zusammenfassung

Die Autoren berichten über einen Fall von Chimärismus beim Menschen, der bei einem Paarling eines verschiedengeschlechtlichen Zwillingspaares beobachtet wurde. Der Chimärismus schien Gewebe- und Blutzellen betroffen zu haben.

Résumé

Description d'une paire de jumeaux bivitellins de sexe différent dont l'un est une chimère. Ceci concerne tout aussi bien des cellules tissulaires que des cellules sanguines.

REFERENCES

1) *Lillie, F. R.:* Science *43:* 611 (1916).
2) *Owen, R. D.:* Science *102:* 400 (1945).
3) *Dunsford, I.; Bowley, C. C.; Hutchison, A. M.; Thompson, J. S.; Sanger, R.* and *Race, R. R.:* Brit. med. J. *ii: 81* (1953).
4) *Ueno, S.; Suzuki, K.* and *Kimura (Yamazawa), K.:* Proc. jap. Med. legal Conf. (June 21, 1957), Jap. J. leg. Med. *11:* 592 (1957).
5) *Booth, P. B.; Plaut, G.; James, J. D.; Ikin, E. W.; Moores, P.; Sanger, R.* and *Race, R. R.:* Brit. med. J. *i:* 1456 (1957).
6) *Nicholas, J. W.; Jenkins, W. J.* and *Marsh, W. L.:* Brit. med. J. *i:* 1458 (1957).
7) *Kuo, K. T.:* Jap. J. leg. Med. *12:* 422 (1958).

Authors' address: Dr. Shokichi Ueno, Dr. Kazuo Suzuki and Dr. Kichihei Yamazawa, Department of Legal Medicine, Faculty of Medicine, University of Tokyo, Hongo, *Tokyo.*

Gregory, I.: Acta genet. *9* : 54—96 (1959)

From The Ontario Hospital, London, Ontario, Canada,
and the Department of Psychiatry, University of Western Ontario, Canada

AN ANALYSIS OF FAMILY DATA ON 1000 PATIENTS ADMITTED TO A CANADIAN MENTAL HOSPITAL

By IAN GREGORY

Introduction

In spite of greatly intensified psychiatric research during the past few decades, a fundamental dichotomy still exists in views on the basic etiology of the major "functional" psychoses, psychoneuroses and other personality deviations. Biologists, physicians and many psychiatrists tend to be committed to a predominantly heredo-constitutional view of these disorders, while other psychiatrists, along with psychologists and social scientists, are more apt to favour environmental hypotheses concerning causation.

Usually the attitude of the individual psychiatrist towards etiology parallels his orientation and training in therapy, and *Hollingshead* and *Redlich* (1958) clearly differentiate many of the characteristics of "directive-organic" psychiatrists from those of their "analytic-psychological" counterparts. However, it appears to the present author quite illogical to argue from the presumptive effects of empirical therapy to causation. Somatic therapies used in psychiatry and the various forms of psychotherapy are alike empirical methods of helping patients, and their apparent success or failure does not indicate whether the maladaptation was initially set in motion by a gene-controlled error in metabolism, or by unfortunate biological or social experiences in the developing organism. For example, it is well known that temporary metabolic imbalance such as deficiency of oxygen, certain vitamins or other essential substances, may produce permanent structural damage or bodily deformity which cannot subsequently be reversed by spontaneous or therapeutic restoration of normal

metabolic function. Such irreversible damage is particularly likely to result from dysfunction affecting immature tissues (e.g. cerebral palsy, rickets or cretinism), but may also occur in the mature organism (e.g. acromegaly).

Part of our current ignorance concerning etiology of mental disorders undoubtedly lies in the complexity of the issues involved, and in insufficiently refined techniques of investigation, but it appears that part also lies in the experiential background and emotional convictions with which the investigator approaches the problems confronting him. Geneticists, neurophysiologists, psychoanalysts and social scientists have tended to confine their investigations to factors with which they are familiar and which appear to them likely to be of importance, while ignoring data which seem of at least equal significance to others. Thus, among many genetic studies of mental abnormality, inadequate attention has been paid to possible environmental influences. This criticism does not apply to investigations into the inheritance of mental ability, and here many of the facts appear to be quite well established (e.g. *Burt*, 1957). The results of ordinary tests of intelligence are distributed among the general population according to the normal or Gaussian curve, and about three-quarters of the total variance is due to genetic factors. *Burt* also points out that several investigations yield fairly clear indications that individual variations in intelligence are influenced by both major genes responsible for comparatively large deviations (usually of an abnormal kind) and multiple genes, the effects of which are small, similar and cumulative.

The role of genetic factors in the etiology of mental deficiency has been ably discussed by several authors (e.g. *Roberts*, 1941, 1950; *Penrose*, 1944; *Slater*, 1944). High grade or "subcultural" mental deficiency appears to correspond with the lower end of the normal distribution curve of intelligence and is transmitted to a similar extent by the influence of multiple genes. The more severe low grade mental deficiency, on the other hand, is usually accompanied by observable brain pathology, frequently environmentally determined (e.g. by anoxia or trauma at birth), but in a few rare disorders resulting from simple Mendelian recessive characteristics (e.g. juvenile amaurotic idiocy, phenylketonuria, true microcephaly and gargoylism).

In the case of mental disorders first manifested in adult life, simple Mendelian inheritance appears to be fairly well established with respect to *Huntington*'s chorea, and has frequently been postulated for the major functional psychoses. Thus, *Kallmann* has repeatedly asserted (1950, 1952, 1953, 1954) that the predisposition to manic depressive psychoses is inherited as a simple autosomal dominant (with incomplete penetrance),

that schizophrenia develops only in individuals homozygous for a simple autosomal recessive characteristic (with other modifying genes), and that involutional psychoses occur principally in schizoid personalities representing the heterozygous genotype of schizophrenia. These conclusions are based essentially on observed frequencies of similar mental disorder in other members of the family greater than in the general population, and on differential frequencies in various family members corresponding with the degree of their genetic similarity to the affected individual. However, geneticists disagree on hypothetical modes of transmission, and *Böök* (1953) considered that the type of schizophrenia prevalent in his investigation area (a North Swedish isolate) was due primarily to a major simple dominant gene with a heterozygous penetrance of about 20 per cent, and a homozygous penetrance of about 100 per cent.

Other authorities in the field of genetics (e.g. *Penrose*, 1950; *Slater*, 1950, 1953; *Sjögren*, 1957) have been more cautious in their interpretations of the facts, and tend to regard each of the functional psychoses, and other personality disorders based on clinical diagnoses, as more or less heterogeneous material, which may include types inherited by various different genetic mechanisms and also types not genetically conditioned. *Slater* (1950) comments on the likelihood that there are aetiological factors, and probably genetical ones, which affect both intelligence and personality. Again *Larsson* and *Sjögren* (1954) note the probability of a genetic connection between oligophrenia and certain psychoses, especially schizophrenia.

In the genetic theory of the major psychoses, considerable significance has been attributed to observed differences between frequencies of similar mental disorders in uniovular and binovular twins of affected individuals. However, it has not always been recognized that such twin studies are open to a number of serious scientific difficulties and objections (e.g. *Neel* and *Schull*, 1954; *Slater*, 1953; *Walker and Reid*, 1955). In his scholarly review of research methods in human genetics, *Penrose* (1950) concludes that theory has advanced beyond the facts, that methods of analysis are available but data have not been supplied, especially in the field of psychiatry. In enumerating the many kinds of observations still required, he comments on the importance of searching for environmental factors modifying genetic effects, and points out that many obvious avenues for research have been neglected, such as the effects of birth order and maternal age on psychotic reactions, and the analysis of variation of abnormal traits within sibships.

In a previous article (*Gregory*, 1958) [a] the present author reviewed a number of studies relating to parental age, family size, birth order and ordinal position; and subjected to further analysis certain data previously

recorded by two other investigators. In another recent article (*Gregory*, 1958[b]) studies on parental deprivation in psychiatric patients have been critically reviewed, and it has been concluded that considerable further investigation is necessary into factual data concerning the families and early experiences of patients with various types of psychatric disorder. The present study is an attempt to provide some objective information along these lines.

Method

Source and nature of data

The basic data recorded and analysed in the present investigation consist of material abstracted from the hospital records of 1,000 consecutive patients born during the years 1906 to 1935 inclusive, and admitted at least once to the Ontario Hospital, London, Canada, during the period July 1st, 1954 to June 12th, 1958. During the past few years, this Hospital has contained over 1,600 patients, and has functioned as the provincial public mental hospital for eight counties in Western Ontario (the counties of Bruce, Dufferin, Grey, Huron, Middlesex, Perth, Waterloo and Wellington). For many years, the hospital has been affiliated with the University of Western Ontario, and has been fully approved for specialist training in psychiatry by the Royal College of Physicians and Surgeons of Canada.

Family and personal histories on each of the patients were recorded routinely shortly after their admission by members of the medical staff, who knew during the latter two years that some investigation of familial data was contemplated, but who were not themselves requested to record any specific familial data in connection with this investigation. Approximately three or four weeks after the patient's admission, the history, clinical findings and program of treatment on each patient were reviewed in some detail at a conference of the medical staff, normally attended by the Superintendent, Assistant Superintendent, and the remaining physicians working on either male or female service, of whom usually two or three had completed their psychiatric training, and the remainder were in process of doing so. The clinical diagnosis on each patient was made at this time (or in a few cases at a later date after representation in a similar conference), and these diagnoses conform with The International Statistical Classification, which is in general use in Canadian Mental Hospitals. Although the present author is skeptical concerning the validity of clinical diagnosis in psychiatry, these diagnoses represent a group decision of educated psychiatric opinion, and have been accepted unchanged for the purpose of the present study. In the event that the patient was admitted and presented in conference more than once during the four year period under examination, the diagnosis made at the most recent conference was the one which has been accepted here.

The majority of these patients were admitted to Hospital on Physicians' Certificates of Mental Illness, but an increasing proportion came on their own voluntary application, and an appreciable percentage were admitted on legal warrants (a number of the latter being found not certifiably mentally defective nor mentally ill and subsequently returning

to the court for disposition). Many of these 1,000 patients had previously been admitted to this or other mental hospitals, and a number were admitted to this Hospital more than once during the four year period under examination. However, every patient born during the period 1900–1935 was included in the study, and each patient only once. No record was included in the study, other than those of patients born during this thirty year period and admitted during the specified four years.

The data recorded here were all abstracted from the Hospital files during the first half of the year 1958. At the outset it was recognized that birth order and ordinal position within the sibships were recorded for about ninety-five percent of patients, and it was considered desirable to obtain this information for as many of the remaining patients as possible, by asking them or responsible informants. Whenever such information was requested (verbally or by letter), information was also sought concerning parental ages at the birth of the patient, and the age of the patient at death or separation of their parents. Such information was then checked against data abstracted from the Hospital records, but little new information was learned and inconsistencies between this and previous information were negligible.

Comparisons undertaken

(i) Tables have been designed to permit comparisons between findings for each of the major diagnostic groups of psychiatric disorders affecting persons aged approximately twenty to fifty years.

(ii) Wherever possible, comparisons have been made between findings for psychiatric patients and those for corresponding members of the general population of Ontario. Data concerning age at marriage, parental ages and illegitimacy were obtained from The Annual Reports of the Registrar General for Ontario (for the years 1921, 1931, 1941 and 1951). Data on mortality (of parents) were calculated from tables contained in Vital Statistics for the year 1951 (published by the Dominion Bureau of Statistics). Data on the number of children ever born per married mother were derived from The Census of Canada for the year 1941.

(iii) Comparisons have been made between observed and statistically expected frequencies of patients according to their birth order, ordinal position in the sibship, and the sexes of their siblings.

The method developed by *Greenwood* and *Yule* (1914) enables the calculation of corrected family sizes, and of expected frequencies of different birth orders, from samples taken through members of the sibships. The present author has previously described a simple extension of this method for estimating expected frequencies of different ordinal positions, and has discussed a number of possible sources of statistical bias in the application of these methods (*Gregory*, 1958[a]). The sample presently under examination consists of patients having a minimum age of eighteen and a half years at the beginning of the four year period (increasing to a minimum of twenty-two and a half years by June 1958), and it is considered that all sibships may be regarded as complete. Only the full live born legitimate siblings are included as members of the sibships (illegitimate patients being grouped with only children or considered separately). In recording birth order, twins were allocated as a $\frac{1}{2}$ to each of two successive birth ranks. Information concerning birth

order and ordinal position was obtained in 96.8 per cent of the total sample, and it is concluded that the methods used provide an accurate picture of the distribution of patients according to size of sibship, birth order and ordinal position.

The present author has not previously examined the frequency of psychiatric disorders in relation to the *sex of siblings*, and some elaboration may, therefore, be necessary of methods used in this connection. Three aspects of the sex of siblings have been investigated, namely (a) the total number of siblings of each sex, (b) the recorded numbers of patients whose siblings were all the same sex as themselves, or all of the opposite sex, (c) the sexes of siblings immediately preceding and following the patient:

(a) Now the general population does not contain equal numbers of persons of each sex, and the proportions of male and female vary in different age groups and from time to time. If the numbers of patients in each diagnostic group were equally divided between the two sexes, it would not be necessary to allow for this differential sex ratio in calculating percentages of total siblings of the same or the opposite sex from the patient. Since the numbers of male and female patients for any given diagnosis differ, however (in some cases very greatly), this source of bias has been obviated by calculating a weighted mean percentage (see table XXIII), which constitutes the average of the percentages for each of the two sexes of patients taken separately. The statistical significance of the deviation of the weighted mean from 50 is obtained by the t test, after calculation of the standard deviation of the sum of the two independent percentages concerned (from the formula

$$\sqrt{(P_1 \times q_1)/n_2 + (P_2 \times q_2)/n_1}).$$

(b) The statistically *expected frequency of patients having all their siblings of the same sex as themselves, or all of the opposite sex*, depends on the size of the sibship of which the patient is a member. In a sibship having x members (where the patient has $x-1$ siblings), the chance that all the siblings will be of the same sex as the patient is approximately the same as the chance that all will be of the opposite sex, and in each case is approximately $\frac{1}{2^{x-1}}$. Now if F_x is the frequency of patients from sibships having x members (including the patient) then the expected frequency of patients having all siblings the same sex as themselves, is approximately the same as the expected frequency of patients having all siblings of the opposite sex, and each is approximately $\frac{F_x}{2^{x-1}}$

(c) For eldest or youngest patients, there are two possible alternatives with regard to the *sex of the preceding or following sibling*. For intermediate patients, there are four possible alternatives (see table XXV), each of which is statistically expected to occur with approximately equal frequency.

The expected frequencies outlined under (b) and (c) depend on the total number of siblings of each sex being approximately equal, as in most diagnostic groups examined here (see table XXIII). If, however, the total numbers of siblings of each sex differed significantly, these expected frequencies could be corrected by weighting them in accordance with the sex distribution of total siblings.

Major diagnostic groups selected

The major diagnostic groups selected for study were schizophrenia, manic depressive psychoses, psychoneuroses, pathological personality, alcoholism, mental deficiency and "other diagnoses".

Four hundred and fifty-three of the patients were diagnosed schizophrenia, and these have been divided into four large sub-groups (those born in Canada during each of three ten year periods, and those born in other countries), which are considered separately in Tables X to XVII.

In all tables except table I, the terms pathological personality, alcoholism and mental deficiency include both categories with psychosis and without psychosis. Thus, pathological personality includes diagnostic class numbers 309.1 and 320, alcoholism includes class numbers 307 and 322, and mental deficiency includes class numbers 309.2 and 325 (see table II).

The results of analysis for each major diagnostic group are now presented as follows

(i) Distribution of patients by sex, year of birth, main socio-cultural characteristics and median age at marriage (tables I to VIII).

(ii) Frequency of surgical experiences, by sex (table IX).

(iii) Frequency of abnormality recorded in parents, full siblings and spouses (table X).

(iv) Parental ages and age differences (tables XI to XIV).

(v) Percentages losing parents by death or permanent separation during childhood, and percentages of illegitimacy (tables XV to XVII).

(vi) Frequency of patients by size of sibship, birth order and ordinal position (tables XVIII to XXII).

(vii) Frequency of patients in relation to the sexes of their siblings (tables XXIII to XXV).

Results

1. Distribution of patients by diagnosis, sex, year of birth, country of birth, religion, education, marital status and median age at marriage (tables I–VIII)

Age sex specific or standardized first admission rates, for selected diagnostic groups and various socio-cultural characteristics, have previously been analyzed in some detail for the two Provincial Mental Hospitals accepting patients from Western Ontario (*Wanklin et al.*, 1955), and for all Canadian Public Mental Hospitals (*Gregory*, 1959).

The figures presented in tables I to VII include both first admissions and re-admissions, and do not represent rates per hundred thousand of the general population, but crude numbers of patients. The purpose of these tabulations is to provide a general picture of the numerical distribution of the 1,000 patients in the present study, according to their diagnosis, sex,

year of birth and main socio-cultural characteristics. It may be noted that approximately two-thirds of all foreign born patients were diagnosed as schizophrenic. About two-thirds of male schizophrenics were single, whereas over two-thirds of female schizophrenics had been married.

Table VIII shows the median age of patients at first marriage and reveals no significant deviations from age at marriage for comparable groups of the general puoplation.

Table I

Diagnostic classes of 1,000 patients, by sex

International statistical classification number	Diagnostic class	Male	*Female*	Both sexes
020.1, 025, 026	Syphilis of central nervous system	3	—	3
300	Schizophrenia	201	*252*	453
301	Manic depressive psychoses	28	*42*	70
302	Involutional melancholia	1	*3*	4
303	Paranoid states	12	*12*	24
305	Presenile psychoses	1	*1*	2
307	Alcoholic psychoses	22	*4*	26
308	Psychoses of other demonstrable aetiology (toxic and organic)	18	*14*	32
309.1	Psychoses with psychopathic personality	6	*4*	10
309.2	Psychoses with mental deficiency	9	*16*	25
309.3	Other and unspecified psychoses	1	*2*	3
310–318	Psychoneuroses	39	103	142
320	Pathological personality	64	*21*	85
321	Immature personality	9	—	9
322	Alcoholism	23	*7*	30
323	Other drug addiction	1	—	1
325	Mental deficiency	30	*20*	50
326	Other disorders of character, behaviour and intelligence	8	*6*	14
353	Epilepsy	2	*5*	7
000	Other non-psychotic diseases	5	*1*	6
793.0	Mental observation without need for further medical care	4	—	4
	All diagnoses	487	*513*	1,000

Table II

Selected diagnostic groups of 1,000 patients, by sex

Diagnostic group	Male	*Female*	Both sexes
Schizophrenia			
born in Canada, 1906–1915	38	*44*	82
born in Canada, 1916–1925	54	*90*	144
born in Canada, 1926–1935	56	*65*	121
foreign born	53	*53*	106
Manic depressive psychoses	28	*42*	70
Psychoneuroses	39	*103*	142
Pathological personality (I.S.C. Nos. 309.1 and 320)	70	*25*	95
Alcoholism (I.S.C. Nos. 307 and 322)	45	*11*	56
Mental deficiency (I.S.C. Nos. 309.2 and 325)	39	*36*	75
Other diagnoses	65	*44*	109
All diagnoses	487	*513*	1,000

Table III

Year of birth of 1,000 patients by diagnosis and sex
Median year of birth, and median age on admission to hospital

Diagnosis	Year of Birth						Median year of birth	Median age on admission to hospital
	1906–1915		1916–1925		1926–1935			
	male	*female*	male	*female*	male	*female*		
Schizophrenia, Canadian born	38	*44*	54	*90*	56	*65*	1921	35 years
Schizophrenia, foreign born	16	*15*	15	*21*	22	*17*	1923	33 years
Manic depressive	18	*16*	5	*16*	5	*10*	1916	40 years
Psychoneuroses	10	*31*	17	*42*	12	*30*	1921	35 years
Pathological personality (309.1, 320)	14	*3*	24	*13*	32	*9*	1924	32 years
Alcoholism (307, 322)	19	*4*	18	*7*	8	—	1917	39 years
Mental deficiency (309.2, 325)	6	*11*	14	*12*	19	*13*	1924	32 years
Other diagnoses	27	*20*	16	*14*	22	*10*	1918	38 years
All diagnoses	148	*144*	163	*215*	176	*154*	1921	35 years

Table IV

Country of birth of 1,000 patients by diagnosis and by sex

Diagnosis	Country of birth							
	Canada		Other British Commonwealth		United States		Other Countries	
	Male	*Female*	Male	*Female*	Male	*Female*	Male	*Female*
Schizophrenia	148	*199*	7	*9*	2	*7*	44	*37*
Manic depressive	24	*35*	1	*1*	—	*2*	3	*4*
Psychoneuroses	36	*83*	2	*13*	—	*2*	1	*5*
Pathological personality (309.1, 320)	62	*21*	2	*3*	1	—	5	*1*
Alcoholism (307, 322)	39	*11*	3	—	2	—	1	—
Mental deficiency (309.2, 325)	39	*30*	—	—	—	*1*	—	*5*
Other diagnoses	51	*34*	2	*4*	—	—	12	*6*
All diagnoses	399	*413*	17	*30*	5	*12*	66	*58*

Table V

Religious denomination of 1,000 patients by diagnosis and by sex

Diagnosis	Religious denomination							
	Selected Protestant Group[1]		Roman Catholic		Other		Not stated	
	Male	*Female*	Male	*Female*	Male	*Female*	Male	*Female*
Schizophrenia, Canadian born	84	*116*	35	*42*	29	*40*	—	*1*
Schizophrenia, foreign born	8	*22*	22	*15*	22	*16*	1	—
Manic depressive	20	*27*	4	*8*	4	*7*	—	—
Psychoneuroses	23	*63*	8	*24*	8	*15*	—	*1*
Pathological personality (309.1, 320)	31	*13*	25	*4*	14	*8*	—	—
Alcoholism (307, 322)	27	*7*	10	*3*	8	*1*	—	—
Mental deficiency (309.2, 325)	23	*20*	9	*7*	6	*9*	1	—
Other diagnoses	27	*26*	19	*14*	18	*4*	1	—
All diagnoses	243	*294*	132	*117*	109	*100*	3	*2*

[1]) The group of protestant denominations selected are Baptist, Church of England, Methodist, Presbyterian, United Church of Canada, and Protestant, denomination unspecified.

Table VI

Education of 1,000 patients by diagnosis and by sex

Diagnosis	Education							
	Public School[1]		High School[1]		University		Not Stated[2]	
	Male	*Female*	Male	*Female*	Male	*Female*	Male	*Female*
Schizophrenia, Canadian born	81	*84*	57	*98*	9	*12*	1	*5*
Schizophrenia, Foreign born	40	*31*	7	*17*	2	*1*	4	*4*
Manic depressive	14	*18*	11	*21*	3	*2*	—	*1*
Psychoneuroses	22	*41*	16	*57*	1	*4*	—	1
Pathological personality (309.1, 320)	48	*14*	14	*9*	3	*2*	5	—
Alcoholism (307, 322)	21	*3*	22	*7*	1	—	1	*1*
Mental deficiency (309.2, 325)	11	*14*	—	—	—	—	28[2]	*22*[2]
Other diagnoses	38	*26*	19	*14*	4	—	4	*4*
All diagnoses	275	*231*	146	*223*	23	*21*	43[2]	*38*[2]

[1]) The group with public school education had appproximately 5–8 years of schooling, while those with high school education had approximately 9–13 years.

[2]) The group for whom education was not stated also contains 25 male and 16 female mental defectives with 0–4 years of schooling.

Data on *multiple births* have not been tabulated, but are as follows. Twins constitute about 1.1 per cent of all births or 2.2 per cent of all children born in Ontario. Of the 1,000 patients studied here, 18 were recorded as having had twin siblings, of which two were stillborn and five more died within the first five years of life. In 3 cases (including the two stillbirths) the sex of the twin was not recorded, and of the remaining 15, 8 were of the same sex as the patient and 7 of the opposite sex. Of the patients themselves, 7 were male and 11 female, and they were distributed among the major diagnostic groups as follows – schizophrenia, Canadian born – 7, foreign born – 1, manic depressive psychoses – 1, psychneuroses – 4, pathological personality – 2, mental deficiency – 1, other diagnoses – 2.

Information concerning consanguinity was not specifically requested in most instances, but a positive history was recorded in four patients, all female. In the case of 2 Canadian born women with paranoid schizophrenia, their parents were reported to be first cousins who had never shown definite abnormality. One other Canadian born schizophrenic was alleged to be the child of a union between her mother and the mother's uncle. The remaining patient, a foreign born schizophrenic, was not herself the product of a consanguineous union, but contracted a marriage with her own uncle.

Table VII

Distribution of 1,000 patients by marital status and by sex

Diagnosis	Marital status							
	Single		Married[1]		Widowed		Divorced	
	Male	*Female*	Male	*Female*	Male	*Female*	Male	*Female*
Schizophrenia, Canadian born	95	*56*	51	*136*	1	*3*	1	*4*
Schizophrenia, Foreign born	36	*12*	17	*39*	—	*1*	—	*1*
Manic depressive	6	*5*	22	*33*	—	*3*	—	*1*
Psychoneuroses	13	*17*	25	*84*	1	*2*	—	—
Pathological personality (309.1, 320)	27	*7*	41	*18*	—	—	2	—
Alcoholism (307, 322)	13	*3*	29	*8*	—	—	3	—
Mental deficiency (309.2, 325)	35	*28*	4	*7*	—	*1*	—	—
Other diagnoses	18	*14*	42	*29*	2	—	3	*1*
All diagnoses	243	*142*	231	*354*	4	*10*	9	*7*

[1]) The Married Group includes those separated but not divorced, and also includes widowed and divorced persons who have remarried.

2. Surgical operations by diagnosis and sex (table IX)

Both sexes show significant differences between observed total numbers of surgical operations recorded for certain diagnoses, and expected frequencies based on average figures for all diagnoses combined. The overall figure for male psychoneurotics is over $1\frac{1}{3}$ times that for all male patients combined, while the overall average for female psychoneurotics is well over $1\frac{1}{2}$ times that for all diagnoses. Both male and female mental defectives and foreign born schizophrenics, on the other hand, are greatly underrepresented. Male manic depressives are in excess of the average for male patients, but this may well be related to a somewhat longer average period of risk, as shown by their age distribution (see table III).

These differences between certain observed and expected total numbers of operations do not appear to be related to abnormally high or low frequencies of certain types of operation alone, but in most instances reflect an overall increase or decrease in the frequency of each different type of operative procedure. However, it may be noted that tonsillectomy was performed with average frequency in the mental defectives, whereas the remaining types of operation tended to be performed less frequently than the average.

Table VIII

Median age at (first) marriage[1], by diagnosis and sex

Diagnosis	Median age at marriage Male		Female	
General population				
married in Ontario, 1931	26.4	years	22.7	years
married in Ontario, 1941	26.3	,,	23.0	,,
married in Ontario, 1951	24.9	,,	22.4	,,
Schizophrenia				
born in Canada, 1906–1915	(29.2)[2]	years	25.2	years
born in Canada, 1916–1925	25.0	,,	21.8	,,
born in Canada, 1926–1935	(21.0)[2]	,,	21.1	,,
foreign born	(28.0)[2]	,,	22.6	,,
Manic depressive psychoses	27.0	,,	23.2	,,
Psychoneuroses	24.9	,,	22.6	,,
Pathological personality	22.8	,,	(20.7)[2]	,,
Alcoholism	23.2	,,	x[3]	
Mental deficiency	x[3]		x[3]	
Other diagnoses	25.0	years	22.4	years

[1] Figures for the general population include all marriages. Figures for patients refer to age at first marriage only, and were recorded in 91 per cent of the patients who had been married (i.e. in 560 out of 615).

[2] These figures are each based on less than 20 observations.

[3] Less than 10 observations recorded.

3. *Recorded frequencies of abnormality in parents, full siblings and spouses (table X)*

Frequencies recorded in Table X represent crude percentages of abnormality recorded in close relatives up till the time of the patient's admission to hospital. The only minor correction that was made in the calculation of these figures was the exclusion of siblings that died before the age of twenty from the total numbers of siblings on which the percentages are based. It should be emphasized, therefore, that the figures for parents are not directly comparable with those for siblings and spouses, since most of the parents have passed through the main period of risk, whereas siblings and spouses have only passed through an approximately equivalent period of risk to the patient. It may be very roughly estimated that at least twice the percentages of siblings and spouses recorded here will eventually manifest each of the types of abnormality recorded.

This table shows the highest frequencies for *suicide* among the fathers of psychotic patients, and the highest frequencies of *admission to mental*

Table IX

Surgical experiences of 1,000 patients, by diagnosis and sex

Diagnosis	Sex	Surgical experiences expressed as percentage of patients in each group						
		Tonsil-ectomy	Append-ectomy	Hernio-raphy	Gynae-cological [1] [2]	Other ab-dominal	Other [4]	All types (Total operations [5]
Schizophrenia,	M	24.3	11.5	5.4	–	0.7	14.2	56.1
born in Canada	*F*	*21.1*	*22.6*	–	*18.1*	*6.0*	*12.5*	*80.3*
Schizophrenia,	M	3.8	11.3	5.7	–	–	9.4	30.2
foreign born	*F*	*20.8*	*15.1*	*1.9*	*7.5*	*3.8*	*9.4*	*58.5*
Manic depressive	M	32.2	17.9	17.9	–	7.2	21.4	96.6
psychoses	*F*	*26.2*	*26.2*	–	*21.4*	–	*11.9*	*85.7*
Psychoneuroses	M	25.6	20.5	7.7	–	–	30.8	84.6
	F	*28.2*	*36.9*	*1.9*	*37.9*	*10.7*	*33.0*	*148.6*
Pathological	M	15.7	24.4	5.7	–	5.7	22.9	74.4
personality	*F*	*32.0*	*32.0*	*8.0*	*28.0*	*8.0*	*12.0*	*120.0*
Alcoholism	M	13.3	17.8	2.2	–	8.9	37.8	80.0
	F [1]	*(27.3)*	*(18.2)*	–	*(9.1)*	–	*(27.3)*	*(81.9)*
Mental	M	20.5	15.4	2.6	–	5.1	7.7	51.3
deficiency	*F*	*19.4*	*2.8*	–	*2.8*	*2.8*	*16.6*	*44.4*
Other diagnoses	M	7.7	18.5	12.3	–	1.5	12.3	52.3
	F	*11.4*	*25.0*	–	*2.3*	*11.4*	*36.4*	*86.5*
All diagnoses	M	17.9	16.2	6.8	–	2.9	18.1	61.9 [5]
	F	*22.6*	*24.2*	*1.0*	*19.1*	*6.4*	*18.9*	*92.2* [5]

[1] There were 25 or more patients in all categories with the exception of female alcoholics, who numbered only 11.

[2] All gynaecological surgery excluding D. & C. and cauterisation of cervix.

[3] A total of 21 female patients were recorded as having had one or more children by Caesarean section, of whom 11 were Canadian born schizophrenics, 1 manic depressive, and 9 psychoneurotic.

[4] A total of 9 patients were reported to have undergone thyroidectomy. Two of these were male patients with pathological personality, and the remainder were female – 1 Canadian schizophrenic, 1 foreign born schizophrenic, 3 manic depressive, 1 psychoneurotic, 1 alcoholic and 1 "other diagnoses".

[5] Goodness of fit between observed and expected *total numbers of surgical operations among male patients* is given by chi-square of 24.04, with 7 degrees of freedom, and hence $0.001 < p < 0.01$. The largest single contribution to chi-square (8.65) was made by foreign born schizophrenics, the next (5.43) by manic depressives, and the next (3.30) by male psychoneurotics.
Goodness of fit between observed and expected *total numbers of surgical operations among female patients* is given by chi-square of 56.71, with 7 degrees offreedom, and hence $p < 0.001$. The largest single contribution to chi-square (35.50) was made by psychoneurotics, the next (8.90) by mental defectives, and the next (6.60) by foreign born schizophrenics.

Table X

Frequency of abnormality recorded in parents[1], full siblings[2] and spouses of 1,000 patients, by diagnosis

Diagnosis	Relationship to patient	Percentage in whom abnormality was recorded at time of patient's admission[1]			
		Suicide	Admission to mental hospital	Excessive consumption of alcohol	Other abnormality recorded
Schizophrenia,	Father	3.7	2.4	8.5	8.5
born in Canada	mother	–	4.9	–	4.9
1906–1915	siblings	0.8	4.7	0.3	6.4
	spouse	–	–	6.0	4.0
Schizophrenia,	father	2.1	3.5	9.7	6.9
born in Canada	mother	–	6.9	–	13.2
1916–1925	siblings	–	3.5	1.1	3.7
	spouse	–	1.1	3.3	6.6
Schizophrenia,	father	0.8	2.5	14.0	11.6
born in Canada	mother	–	9.9	0.8	15.7
1926–1935	siblings	0.4	3.7	0.4	6.1
	spouse	–	3.7	7.4	11.1
Schizophrenia,	father	0.9	0.9	7.5	9.4
foreign born	mother	0.9	1.9	–	4.7
	siblings	–	2.2	0.3	3.9
	spouse	–	–	14.3	7.1
Manic depressive	father	2.9	5.7	7.1	4.3
psychoses	mother	1.4	7.1	–	10.0
	siblings	1.3	5.6	0.4	6.5
	spouse	1.7	–	6.5	1.7
Psychoneuroses	father	1.4	3.5	9.1	7.8
	mother	–	3.5	0.7	18.3
	siblings	–	2.3	0.6	5.8
	spouse	–	1.8	6.4	11.9
Pathological	father	–	1.0	14.7	6.3
personality	mother	–	2.1	5.3	12.6
(309.1, 320)	siblings	0.9	0.9	2.6	2.8
	spouse	–	–	6.6	13.1
Alcoholism	father	–	–	23.2	1.8
(307, 322)	mother	–	1.8	1.8	3.6
	siblings	–	0.5	4.2	1.0
	spouse	–	–	2.5	10.0
Mental deficiency	father	–	1.3	9.3	6.7
(309.2, 325)	mother	1.3	1.3	1.3	13.3
	siblings	–	0.3	–	9.8
	spouse	–	–	–	–
Other diagnoses	father	2.7	0.9	8.2	5.5
	mother	–	2.7	–	3.7
	siblings	0.3	1.1	1.9	3.6
	spouse	–	1.3	1.3	10.5

[1] Note that the figures for parents are not directly comparable with those for siblings and spouses, since the parents have passed through a much longer period of risk.

[2] Siblings dying before the age of 20 years have been excluded from the total numbers of siblings on which these percentages are based.

hospital among the mothers of psychotic patients (maximal for the *youngest* group of schizophrenics). The highest frequencies for *excessive consumption of alcohol* were recorded among the fathers of the youngest group of schizophrenics, of patients with pathological personality, and of patients with alcoholism (maximal in the last named).

Significant percentages of the full siblings of psychotic patients had already been admitted to mental hospital, while appreciable percentages of the siblings of patients with pathological personality and alcoholism were already drinking excessively.

Table XI

Median ages of parents at birth of patients and median parental age differences, by diagnosis[1]

Diagnosis	Number of cases recorded (N)[1]	Median age of father at birth	*Median age of mother at birth*	Median difference in ages of parents
General population[2]				
born in Ontario, 1921	72,560	32.6 years	*28.7 years*	3.9 years
born in Ontario, 1931	66,436	31.8 „	*28.1* „	3.7 „
Schizophrenia				
born in Canada, 1906–1915	50	33.5 years	*28.8 years*	4.7 years
born in Canada, 1916–1925	104	35.7 „ [4]	*31.5* „ [5]	4.2 „
born in Canada, 1926–1935[3]	94	33.9 „	*30.0* „ [6]	3.9 „
foreign born	70	33.4 „	*29.5* „	3.9 „
Manic depressive psychoses	53	33.7 „	*31.5* „	2.2 „
Psychoneuroses	106	33.6 „	*29.8* „	3.8 „
Pathological personality	63	31.7 „	*28.5* „	3.2 „
Alcoholism	38	33.0 „	*30.3* „	2.7 „
Mental deficiency	50	38.0 „ [5]	*31.7* „ [4]	6.3 „
Other diagnoses	67	32.9 „	*28.9* „	4.0 „

[1] For 695 patients (out of the total sample of 1,000) for whom ages of both father and mother were obtainable.

[2] Calculated from data on legitimate liveborn children born in Ontario (Registrar-General's annual reports relating to the registration of Births, Marriages and Deaths in the Province of Ontario, for the years 1921 and 1931).

[3] Of the 121 *schizophrenics born in Canada 1926–1935* (56 male and 65 female), there were 92 for whom *education and the ages of both parents at birth* were recorded. For 37 patients with public school education (5–8 years), the median age of father at birth was 34.75, and the median age of mother 31.25 years. For 55 patients with 9 years or more of schooling the median age of father at birth was 34.17, and the median age of mother 28.75 years.

[4] Significant ($P<0.01$)

[5] Extremely significant ($P<0.001$)

[6] Probably significant ($P<0.05$)

The spouses with the highest previous frequency of admission to mental hospital were those of the *youngest* group of schizophrenics, while the spouses with the highest frequency of excessive drinking were those of the foreign born schizophrenics.

4. Parental ages and age differences (tables XI–XIV)

Tables XI and XII show significant increases in mean and median ages of both parents for the two largest groups of schizophrenic patients, and also for mental deficiency. It is considered possible (but not demonstrated here) that such observations may be related to education and social status (of parents and/or patients).

Table XIII shows some suggestive increases in the percentage of certain patients with mothers older than their fathers, or with fathers at least ten years older than their mothers. However, for the youngest group of schizophrenic patients, such differences appeared to be extremely significantly related to the duration of the patient's education (table XIII, footnote [3]).

Table XII

Means and standard deviations of parental ages at birth of patients, by diagnosis[1]

Diagnosis	Number of cases recorded (N)[1]	Age of father at birth Mean	S. D.	*Age of mother at birth Mean*	*S. D.*
General population[2]					
born in Ontario, 1921	72,560	33.6 years	7.3 years	*30.0 years*	*6.2 years*
born in Ontario, 1931	66,436	32.9 „	7.2 „	*28.7 years*	*6.1 years*
Schizophrenia					
born in Canada, 1906–1915	50	35.1 years	7.2 years	*29.6 years*	*6.7 years*
born in Canada, 1916–1925	104	36.1 „ [3]	7.5 „	*31.4 „*	*6.3 „*
born in Canada, 1926–1935	94	35.5 „ [3]	8.8 „	*30.4 „* [4]	*7.0 „*
foreign born	70	34.5 „	7.2 „	*29.7 „*	*6.8 „*
Manic depressive psychoses	53	34.2 „	6.8 „	*30.4 „*	*5.7 „*
Psychoneuroses	106	34.2 „	7.7 „	*30.3 „*	*6.5 „*
Pathological personality	63	34.5 „	10.0 „ [3]	*29.1 „*	*7.1 „*
Alcoholism	38	34.3 „	7.7 „	*29.5 „*	*6.4 „*
Mental deficiency	50	37.1 „ [3]	8.4 „	*33.0 „* [3]	*7.1 „*
Other diagnoses	67	32.5 „	7.1 „	*29.4 „*	*6.5 „*

[1] [2] See footnotes [1] and [2] beneath table X

[3] Significant ($P<0.01$)

[4] Probably significant ($P<0.05$)

Table XIV indicates that the observed increases in parental ages are *not* related to the age of the parent being recorded more frequently for dead parents than for living ones.

5. Percentages losing parents by death or permanent separation during childhood, and percentages of illegitimacy (tables XV–XVII)

Table XV shows the cumulative percentages of the general population losing either parent by death during childhood, and illustrates how such figures are related to year of birth (as well as the age and sex of the parent). Now it has already been noted that the average age of father was slightly

Table XIII

Percentage distribution of patients, according to age difference between parents, by diagnosis[1]

Diagnosis	Number of cases recorded (N)[1]	Percentage distribution of patients by age difference between parents: Mother recorded as older than father	Father not more than 10 years older than mother	Father at least 10 years older than mother	Total
General population[2]					
born in Ontario, 1921	72,560	11.9	75.8	12.3	100
born in Ontario, 1931	66,436	11.9	75.1	13.0	100
Schizophrenia					
born in Canada, 1906–1915	50	18.4	59.1	22.5	100
born in Canada, 1916–1925	104	11.6	72.9	15.5	100
born in Canada, 1926–1935[3]	94	10.7	69.1	20.2	100
foreign born	70	10.1	69.7	20.2	100
Manic depressive psychoses	53	24.6[4]	60.3[4]	15.1	100
Psychoneuroses	106	13.3	71.5	15.2	100
Pathological personality	63	9.5	69.9	20.6	100
Alcoholism	38	10.5	73.7	15.8	100
Mental deficiency	50	18.0	58.0[4]	24.0	100
Other diagnoses	67	13.4	82.1	4.5[5]	100

[1] [2] See footnotes [1] and [2] beneath table X

[3] Of the 121 *schizophrenics born in Canada 1926-1935* (56 male and 65 female), there were 92 for whom *education and the ages of both parents at birth* were recorded. Among 37 patients with public school education (5–8 years), there were 7 (18,9%) whose mothers were older than father, 17 (46.0%) whose fathers were not more than 10 years older, and 13 (35.1%) whose fathers were at least 10 years older than mother. Out of 55 patients with 9 years or more of schooling these figures were 2 (3.6%), 47 (85.5%) and 6 (10.9%) respectively. The difference between the two percentages whose fathers were 0–9 years older than their mothers is 39.6 ± 9.45. Hence $\tau = 4.18$, and $p < 0.001$.

[4] Probably significant ($p < 0.05$)

[5] Significant ($p < 0.01$)

under 35, and the average age of mother approximately 30, at the birth of patients in most diagnostic groups, so that the expected frequencies of their losing either parent by death during childhood approximately correspond with the figures presented in Table XV.

Table XIV

Percentages of living and dead parents whose age was obtainable, by diagnosis of patient

Diagnosis	Percentage of living parents whose age was obtainable	Percentage of dead parents whose age was obtainable
Schizophrenia, born in Canada	81.5	72.0
Schizophrenia, foreign born	72.5	61.5
Manic depressive psychoses	88.0	75.5
Psychoneuroses	88.5	66.5
Pathological personality	76.0	73.5
Alcoholism	77.5	74.0
Mental deficiency	83.0	67.5
Other diagnoses	80.0	61.0

Table XV

Cumulative percentages of selected Ontario born General population losing either parent, by death during childhood[1] [2]

Year of Child's Birth	Age of Child by which parent had died	Loss of Father[2] [3]	Loss of Mother[2] [3]
1921	birth	0.4	–
	5 years	2.6	2.1
	10 years	5.5	4.3
	15 years	8.8	6.5
	20 years	13.6	9.1
1931	birth	0.4	–
	5 years	2.2	1.6
	10 years	4.5	3.2
	15 years	7.7	4.9
	20 years	12.4	7.1

[1] Obtained by actuarial computation from age sex specific death rates for the province of Ontario, 1921–1951, published by the Dominion Bureau of Statistics, 1951.

[2] Calculations were based on an assumed paternal age of 35 years and maternal age of 30 years at the birth of the child (in either 1921 or 1931) – see tables XI and XII.

[3] If f is the percentage losing a father, and m is the percentage losing a mother, then the percentage losing *both parents* is fm/100, and the percentage losing *either or both parents* is f+m—(fm/100).

Table XVI

Cumulative percentages of patients losing parents by death or permanent separation during childhood

Diagnosis	Age by which parent lost	Loss of first Parent				Loss of second parent	
		by death only		by death or permanent separation		by death only	by death or permanent separation
		Father	*Mother*	Father	*Mother*		
Schizophrenia	birth	–		–	–	–	–
born in Canada	5 years	3.7	*4.9*	4.3	*5.5*	–	2.4
1906–1915	10 years	8.5	*7.3*	9.1	*7.9*	–	3.7
	15 years	14.6	*9.7*	15.3	*10.4*	–	4.9
	20 years	15.9	*11.0*	16.5	*11.6*	2.4	7.3
Schizophrenia	birth	–	–	1.4	–	–	–
born in Canada	5 years	3.5	*5.5*	6.9	*5.5*	–	5.5
1916–1925	10 years	5.5	*7.6*	10.7	*8.0*	–	8.3
	15 years	6.2	*10.4*	13.5	*11.4*	–	8.3
	20 years	11.1	*11.8*	18.4	*13.5*	–	8.3
Schizophrenia	birth	–	–	1.6	–	–	–
born in Canada	5 years	4.9	*2.5*	8.7	*2.9*	–	3.3
1926–1935	10 years	9.1	*4.9*	12.8	*5.4*	0.8	6.6
	15 years	12.4	*4.9*	17.8	*7.8*	0.8	7.4
	20 years	14.9	*7.4*	21.9	*11.1*	2.5	9.9
Schizophrenia	birth	–	–	1.9	–	–	–
foreign born	5 years	4.7	*4.7*	8.5	*4.7*	1.9	4.7
	10 years	10.4	*8.5*	18.4	*8.9*	1.9	5.6
	15 years	13.6	*12.7*	23.6	*13.2*	3.8	10.4
	20 years	19.8	*13.2*	30.1	*14.1*	5.6	15.0
Manic	birth	–	–	–	–	–	–
depressive	5 years	4.6	*0.4*	5.0	*0.7*	*0.7*	*0.7*
psychoses	10 years	7.5	*1.8*	9.3	*2.1*	0.7	0.7
	15 years	10.4	*4.7*	13.6	*6.4*	2.1	2.1
	20 years	14.7	*7.5*	20.7	*9.3*	3.6	5.0
Psycho-	birth	1.4	–	3.5	–	–	–
neuroses	5 years	5.6	*2.8*	10.6	*2.8*	1.4	4.9
	10 years	7.7	*6.3*	14.1	*6.3*	1.4	5.6
	15 years	9.8	*8.4*	17.6	*9.1*	1.4	5.6
	20 years	11.2	*10.5*	19.0	*11.2*	2.1	5.6
Pathological	birth	–	–	5.3	–	–	–
	5 years	3.2	*1.1*	12.6	*3.2*	1.1	7.4
personality	10 years	5.3	*4.2*	16.9	*7.4*	2.1	10.5
(309.1, 320)	15 years	6.3	*8.4*	20.6	*13.2*	2.1	12.6
	20 years	6.3	*9.5*	20.6	*14.2*	2.1	13.7
Alcoholism	birth	–	–	3.6	–	–	–
(307, 322)	5 years	–	*3.6*	11.6	*4.5*	–	5.4
	10 years	1.8	*5.4*	15.2	*8.0*	1.8	7.1
	15 years	5.4	*10.7*	18.8	*13.4*	1.8	10.7
	20 years	7.1	*10.7*	22.4	*13.4*	1.8	10.7
Mental	birth	1.3	–	4.0	–	–	–
deficiency	5 years	1.3	–	4.7	*0.7*	–	1.3
(309.2, 325)	10 years	2.7	*1.3*	6.0	*2.0*	–	1.3
	15 years	5.3	*8.0*	8.7	*10.0*	–	2.7
	20 years	9.3	*9.3*	12.7	*11.3*	–	2.7
Other	birth	–	–	4.6	–	–	–
diagnoses	5 years	2.7	*3.7*	8.2	*3.7*	*0.9*	6.4
	10 years	7.3	*5.5*	12.8	*5.5*	0.9	6.4
	15 years	11.9	*8.2*	17.4	*8.2*	1.8	7.3
	20 years	12.8	*9.2*	18.3	*9.2*	1.8	7.3

Table XVII

Percentages of patients recorded as illegitimate, by diagnosis

Diagnosis	Percentage recorded as illegitimate
General population	
born in Ontario, 1911	1.9
born in Ontario, 1921	2.1
born in Ontario, 1931	4.0
Schizophrenia	
born in Canada, 1906–1915	None recorded
born in Canada, 1916–1925	1.4 ± 1.0
born in Canada, 1926–1935	1.6 ± 1.2
foreign born	1.9 ± 1.3
Manic depressive psychoses	None recorded
Psychoneuroses	2.1 ± 1.2
Pathological personality	5.3 ± 2.3
Alcoholism	3.6 ± 2.5
Mental deficiency	2.7 ± 1.9
Other diagnoses	4.6 ± 2.0
All diagnoses	2.3 ± 0.5

The figures in table XV may be expected to be somewhat *higher* than the figures in the first two columns of Table XVI for two reasons – (i) an unknown number of parents from whom the patient is permanently separated will have subsequently died without this fact being recorded. (ii) the figures in the first two columns of Table XVI refer only to the loss of the *first* parent by death, and differ from those in table XV by at least the (relatively small) percentages in the fifth column of table XVI which refer to the loss of the *second* parent by death.

Nevertheless, close examination of table XVI gives some indications of the type and frequency of parental deprivation in psychiatric patients, and also the sex of the parent more frequently lost. Standard errors have been omitted from table XVI, partly for the sake of clarity, and partly because most of the findings discussed below are suggestive rather than statistically significant. However, the standard error may readily be calculated from the formula $\sqrt{\frac{p \times q}{n}}$, where p is the percentage who have lost a parent, q the percentage who have not done so, and n the total number of patients in each group (as given in table II).

For most groups of psychiatric patients father was (first) lost by death more frequently than mother (as in the general population), and *for all*

groups of patients permanent loss of father from all causes was more frequent than permanent loss of mother.

Death of father before the age of 10 years exceeded the expected frequency in the youngest schizophrenic group, in manic depressive psychoses and psychoneuroses. *Death of mother before the age of 10 years* exceeded the expected frequency in all schizophrenic groups.

The loss of the first parent by permanent separation was relatively most frequent for patients with psychoneursoses, pathological personality and alcoholism. While the percentages of these three groups losing a parent by death or separation by the age of 20 each exceeded 30%, however, such comparative figures as are available suggest there may be a similarly high expectancy in at least certain groups of the general population (*Gregory*, 1958 [b]). Nevertheless, the relatively high percentages of these patients losing a father permanently during the first decade of life (over 10%, excluding the illegitimate) are suggestive.

The percentages of patients losing a second parent by death appear to be compatible with expected figures obtained by applying the formula $\frac{m \times f}{100}$ to either the figures in table XV or the first two columns in table XVI (see table XV, footnote [3] for the derivation of this formula). However, the figures for *loss of a second parent from all causes* (given in the last column of table XVI, are greatly in excess of expected figures derived from the application of this formula to the third and fourth columns in this table. In the case of mental deficiency, the observed frequency is slightly less than twice the expected, in manic depressive psychoses and psychoneuroses over $2\frac{1}{2}$ times the expected, and for all remaining diagnoses more than 3 times the expected (in pathological personality almost 5 times the expected figure).

The percentages of patients recorded as *illegitimate* may be obtained by differencing the first and third columns in table XVI, but for the sake of clarity are listed separately in table XVII.

6. Distribution of patients by corrected size of sibship, birth order and ordinal position (tables XVIII–XXII)

Table XVIII shows birth order and size of sibship for 453 patients with schizophrenia (all four groups combined), and table XIX shows the reconstruction of their sibships according to the *Greenwood-Yule* method, and the extension previously described for examining ordinal position (*Gregory*, 1958 [a]).

Similar tables to these two were constructed for each of the remaining

Table XVIII

Birth order and size of sibship for 453 patients with schizophrenia[1] [2]

Birth order	Size of sibship (x) 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Not recorded	Total
1	30[1])	22½	15½	17	8	7	2	5	2	1	2	–	1	–	–	–	–	113
2		19½	25½	15	13½	11	–	3	3	1	1	2	–	1	–	–	–	95½
3			25	20	10½	5	2	3	–	1	1	–	–	–	–	1	–	68½
4				20	14	8	4	2	1	4	2	–	–	–	–	–	–	55
5					9	13	4	2½	2	4	–	–	–	–	–	1	–	35½
6						7	3	5½	2	–	1	–	–	–	1	–	–	19½
7							2	6	3	2	–	–	1	–	1	1	–	16
8								5	3	2	–	–	1	–	–	–	–	11
9									8	–	1	1	–	–	–	–	–	10
10										1	1	1	–	–	–	–	–	3
11											1	2	–	–	1	–	–	4
12												3	1	–	–	–	–	4
13																		–
14														1	–	–	–	1
15																–	–	–
16																1	–	1
Not recorded	–	2	1	1	3	1	–	–	1	–	–	–	–	–	–	–	7	16
Total (Fx)	30	44	67	73	58	52	17	32	25	16	10	9	4	2	3	4	7	453

[1] 6 patients were reported to be illegitimate, and are here included with the only children.

[2] The fractions are due to twins, which have been allocated as ½ to each of two successive birth orders.

Table XIX

Reconstruction of sibships of 437 patients with schizophrenia for whom birth order was recorded

Size of sibship ($\varkappa$)	Frequency of sibship recorded in sample of patients ($F\varkappa$)	Weighted frequency (as would have been obtained from sample of mothers) ($F\varkappa/\varkappa$)	Expected frequency of each birth order (summing $F\varkappa/\varkappa$ from bottom upward) ($E\varkappa$)	Observed frequency of each birth order ($O\varkappa$)	$\frac{(O\varkappa - E\varkappa)^2}{E\varkappa}$
1	30	30.0	123.76	113	0.94
2	42	21.0	93.76	95.5	0.03
3	66	22.0	72.76	68.5	0.25
4	72	18.0	50.76	55	0.36
5	55	11.0	32.76	35.5	0.23
6	51	8.5	21.76	19.5	0.23
7	17	2.43	13.26	16	0.57
8	32	4.0	10.83	11	0.00
9	24	2.67	6.83	10	1.81
10	16	1.6	4.16	3	
11	10	0.91	2.56	4	
12	9	0.75	1.65	4	
13	4	0.31	0.9	0	
14	2	0.14	0.59	1	
15	3	0.2	0.45	0	
16	4	0.25	0.25	1	
Totals	437	123.76	437.04	437	4.42

Characteristics of corrected family size ($F\varkappa / \varkappa$)

Mode = 1
Median = 2.49
Mean = 3.54

Goodness of fit of expected and observed frequencies of *birth order*

Chi-square = 4.42
degrees of freedom = 8
$\therefore 0.80 < p < 0.90$

Ordinal position in sibship *for patients from sibships having four or more members*	Expected frequency (Ep)	Observed frequency (Op)	$\frac{(Op - Ep)^2}{Ep}$
Eldest	50.76	45	0.65
Second born	50.76	50½	0.00
Intermediate	95.96	82½	1.89
Penultimate	50.76	63	2.96
Youngest	50.76	58	1.03
Totals	299.00	299	6.53

Goodness of fit for *ordinal position* in sibships with four or more members
$\chi^2 = 6.53$
d. f, = 4
$\therefore 0.10 < p < 0.20$

Table XX

Corrected size of sibship (family of origin), for apparently legitimate patients, by diagnosis[1] [2]

Diagnosis	Total cases in samples of affected siblings (i.e. patients) $\Sigma(F\varkappa)$	Weighted totals (as if obtained from samples of mothers) $\Sigma(F\varkappa/\varkappa)$	Corrected mean size of sibship (as if obtained from samples of mothers)[3]	Percentage distribution by corrected size of sibship, as if obtained through samples of mothers (percentage distribution of $F\varkappa/\varkappa$)						
				1	2	3	4	5	6–9	10 and over
General population (children ever born to Ontario mothers ever married, and aged 45–54 years in 1941)	—	164,751	3.75	18.2	21.9	17.9	13.0	8.9	15.3	4.8
Schizophrenia,										
born in Canada, 1906–1915	80	18.9	4.2	10.6	15.9	22.6	13.2	13.8	16.5	7.4
born in Canada, 1916–1925	142	35.4	4.0	16.9	12.7	16.9	19.8	13.0	16.7	4.0
born in Canada, 1926–1935	117	36.4	3.2	24.8	27.5	13.7	11.5	7.1	12.4	3.0
foreign born	101	29.7	3.4	23.6	15.1	23.6	15.1	6.1	14.8	1.7
Manic depressive psychoses[4]	70	22.8	3.1	30.8	19.7	16.2	9.6	11.4	9.7	2.6
Psychoneuroses[4]	138	46.5	3.0	34.5	21.5	13.5	9.0	6.0	13.6	1.9
Pathological personality[4]	89	27.4	3.2	32.9	14.6	18.2	10.9	8.7	11.6	3.1
Alcoholism[4])	53	15.5	3.4	25.8	19.4	12.9	16.2	6.4	18.7	0.6
Mental deficiency	73	21.7	3.4	18.4	34.6	13.8	7.8	8.3	13.4	3.7
Other diagnoses[4]	101	30.2	3.3	23.2	19.9	19.9	14.9	7.3	11.5	3.3

[1] Size of sibship was recorded for 964 out of 977 patients who were apparently legitimate children.

[2] In calculating standard errors (and hence statistical significance) of corrected mean sizes of sibships and percentages of only children (both of which are derived from the weighted distribution $F\varkappa/\varkappa$), it was decided to err on the conservative side by using the figure $\Sigma(F\varkappa/\varkappa)$ as the total number of observations (N), so that estimates of standard errors would be maximal *(McKeown and Record* (1957), quoted by *Gregory*, 1958a). None of the results quite reach statistical significance.

[3] The corrected mean size of sibship (family of origin), as if obtained through a sample of mothers, is given by the formula $\Sigma(F\varkappa)/\Sigma(F\varkappa/\varkappa)$.

[4] In comparing means and modes of live children ever born per married mother for about 50 samples of British mothers (by year of marriage, age at marriage, and broad social status group), the present author found empirically that with a mode of 1 the mean did not exceed 2.6 in any instance *(Gregory*, 1958a, table VIII).

Table XXI

Goodness of fit between expected and observed frequencies of each *birth order*, by diagnosis[1]

Diagnosis	Number of observations (N)	Goodness of fit between expected and observed frequencies of *birth order*		
		Chi-square	Degrees of freedom	Probability
Schizophrenia (all groups)	437	4.42	8	$0.80<p<0.90$
Manic depressive psychoses	70	1.76	3	$0.50<p<0.70$
Psychoneuroses	138	1.80	4	$0.70<p<0.80$
Pathological personality	92	1.46	3	$0.50<p<0.70$
Alcoholism	55	1.54	2	$0.30<p<0.50$
Mental deficiency	73	2.46	2	$0.20<p<0.30$
Other diagnoses	103	5.43	4	$0.20<p<0.30$

[1] Birth order was recorded in 968 out of 1,000 patients.

Table XXII

Goodness of fit between expected and observed frequencies of each *ordinal position*[1] [2] *in sibships having four or more members*, by diagnosis

Diagnosis	Number of observations (N)	Goodness of fit between expected and observed frequencies of ordinal position in sibships with four or more members		
		Chi-square	Degrees of freedom	Probability
Schizophrenia (all groups)	299	6.53	4	$0.10<p<0.20$
Manic depressive psychoses	43	0.33	2	$0.80<p<0.90$
Psychoneuroses	80	3.77	4	$0.30<p<0.50$
Pathological personality	56	1.00	2	$0.50<p<0.70$
Alcoholism	37	1.37	2	$0.50<p<0.70$
Mental deficiency[3])	45	7.02	2	$0.02<p<0.05$[3]
Other diagnoses	62	3.73	4	$0.30<p<0.50$

[1] Ordinal position was recorded in 968 out of 1,000 patients.

[2] Eldest, second born, intermediate, penultimate and youngest.

[3] The findings with respect to mental deficiency are related to a relative excess of penultimate and youngest children who numbered 9 and 12 respectively (expected frequency 6.73 in each instance). Now, of the 45 mental defectives from sibships having four or more members, 7 were diagnosed as mongols, of whom 5 were last born and 2 penultimate.

six diagnostic groups of patients, but have not been reproduced in the present article.

The percentage distribution of each diagnostic group by *corrected size*

Table XXIII

Percentage distribution by sex of all siblings[1] of psychiatric patients, by diagnosis

Diagnosis	Sex of patient	Percentage distribution of siblings according to their sex		Statistical significance of deviations in weighted means[2]
		Siblings of same sex as patient	Siblings of opposite sex from patient	
Schizophrenia, all groups	Male	53.8	46.2	
	Female	48.5	51.5	
	weighted mean (both sexes)	*51.15*	*48.85*	$\tau = 0.85$ $\therefore 0.30<p<0.40$
Manic depressive psychoses	Male	62.2	37.8	
	Female	46.5	53.5	
	weighted mean (both sexes)	*54.35*	*45.65*	$\tau = 1.25$ $\therefore 0.20<p<0.30$
Psychoneuroses	Male	59.2	40.8	
	Female	49.7	50.3	
	weighted mean (both sexes)	*54.45*	*45.55*	$\tau = 1.67$ $\therefore 0.05<p<0.10$
Pathological personality	Male	53.8	46.2	
	Female	41.7	58.3	
	weighted mean (both sexes)	*47.75*	*52.25*	$\tau = 0.74$ $\therefore 0.40<p<0.50$
Alcoholism	Male	60.4	39.6	
	Female	60.0	40.0	
	weighted mean (both sexes)	*60.2*	*39.8*	$\tau = 1.74$ $\therefore 0.05<p<0.10$
Mental deficiency	Male	46.8	53.2	
	Female	50.9	49.1	
	weighted mean (both sexes)	*48.85*	*51.15*	$\tau = 0.37$ $\therefore 0.70<p<0.80$
Other diagnoses	Male	48.6	51.4	
	Female	62.6	37.4	
	weighted mean (both sexes)	*55.6*	*44.4*	$\tau = 2.00$ $\therefore 0.02<p<0.05$

[1] The sex of 23.9% of all siblings was not recorded (i.e. for 957 out of 4,004 siblings).

[2] The standard error of the sum (or difference) of the two percentage for siblings of the same sex as the patient, or siblings of the opposite sex from the patient, is given by the formula $\sqrt{(p_1 \times q_1)\, n_1 + (p_2 \times q_2)\, n_2}$, and τ is the deviation of this sum from 100 divided by the standard error of the sum. The weighted mean is the sum of the two percentages divided by two.

of family (the weighted distribution F_x/x which would have been obtained from a sample of mothers), excluding all illegitimate patients, is given in table XX, which also shows a comparable distribution for the general

Table XXIV

Expected[1] and observed[2] numbers of patients having siblings all the same or all the opposite sex, by diagnosis

Diagnosis			Numbers of patients with siblings all the same or all the opposite sex, according to size of sibship (x)				
			2	3	4	5	6
Schizophrenia, all groups[3])	*expected*		*22.0*	*16.75*	*9.125*	*3.625*	*1.625*
	observed	all same sex	18	20	8	3	1
		all opposite	26	10	8	1	3
Manic depressive psychoses	*expected*		*4.5*	*2.75*	*1.125*	*0.81*	*0.19*
	observed	all same sex	1	4	1	1	0
		all opposite	8	2	0	1	0
Psycho-neuroses	*expected*		*10.0*	*4.75*	*2.125*	*0.875*	*0.69*
	observed	all same sex	15	4	3	0	3
		all opposite	5	5	4	0	1
Pathological personality	*expected*		*4.0*	*3.75*	*1.5*	*0.75*	*0.125*
	observed	all same sex	4	2	2	0	0
		all opposite	3	5	1	0	0
Alcoholism	*expected*		*3.0*	*1.5*	*1.25*	*0.31*	*0.29*
	observed	all same sex	3	2	2	2	1
		all opposite	3	2	3	0	0
Mental deficiency	*expected*		*7.5*	*2.25*	*0.875*	*0.62*	*0.22*
	observed	all same sex	7	2	0	1	0
		all opposite	8	0	0	1	0
Other diagnoses	*expected*		*6.0*	*4.5*	*2.25*	*0.69*	*0.25*
	observed	all same sex	3	5	4	1	1
		all opposite	9	4	0	0	0

[1] The expected number of patients having either all their siblings the same sex as themselves, or all their siblings the opposite sex, is $F_x 2^{(x-1)}$, where x is the size of the sibship, and F_x is the frequency of patients from sibships having x members (including themselves).

[2] It was not recorded whether siblings were all the same sex, all the opposite sex, or of mixed sexes, in 15.9% of patients having one or more siblings (i.e. 144 out of 906).

[3] The goodness of fit between expected and observed frequencies for schizophrenia (all groups) is given by chi-square of 5.63, with 3 degrees of freedom, and hence $0.10 < p < 0.20$.

population. It will be noted that the mean size of family of origin tends to be about average for the comparable schizophrenic group (born in Canada 1916–1925), but lower for the remaining diagnoses, particularly manic depressive psychoses, psychoneuroses and pathological personality. The modal size of family for each of these three diagnoses is 1, which differs from the empirical expectation for families of mean size over 2.6. Moreover, the percentage of only children in these diagnostic groups considerably exceeds the percentage for the general population.

Table XXI is a summary of the results obtained by examining the distribution of patients according to their *birth order*, and shows no significant differences between observed and expected frequencies in any diagnostic category.

Table XXV

Sexes of siblings immediately preceding and following psychiatric patients, by diagnosis[1]

Diagnosis	Ordinal position of patient							
	Oldest		Youngest		Intermediate			
	Followed by sibling of:–		Preceded by sibling of:–		Preceded by sibling of same sex and followed by sibling of:–		Preceded by sibling of opposite sex and followed by sibling of:–	
	Same sex	Opposite sex	Same sex	Opposite sex	Same sex	Opposite sex	Same sex	Opposite sex
Schizophrenia, all groups	36	32	37	35	37[2]	43[2]	28[2]	27[2]
Manic depressive psychoses	6	5	3	9	5	4	8	3
Psychoneuroses	11	7	15	8	14[3]	6[3]	19[3]	5[3]
Pathological personality	9	7	4	5	6	8	7	9
Alcoholism	5	5	3	4	7	4	3	2
Mental deficiency	3	6	7	12	7	4	4	5
Other diagnoses	6	11	10	5	9	7	5	11

[1] This information was not recorded in 33% of patients having one or more siblings (i.e. in 303 out of 906).

[2] For the 135 *intermediate schizophrenic patients*, the expected figure in each of the four sub-groups is approximately insert 33.75. Goodness of fit between expected and observed figures is given by chi-square = 5.2, with 3 degrees of freedom, and hence $0.10 < p < 0.20$. However, it may also be noted that the percentage of intermediate schizophrenic patients *preceded by a siblings of the same sex* is 59.3 (± 4.23). The significance of the deviation of this percentage from 50 may be obtained b $\tau = 2.20$, and hence $0.02 < p < 0.05$.

[3] For the 44 *intermediate psychoneurotic patients*, the expected figure in each of the four sub-groups is approximately insert 11. Goodness of fit between expected and observed figures is given by chi-square = 12.2, with 3 degrees of freedom, and hence $0.001 < p < 0.01$

Table XXII is a similar summary of the results obtained by examining distributions according to *ordinal position of patients from sibships having four or more members*. The only probable significant difference between observed and expected frequencies was found in the case of *mental deficiency*, where the last born and penultimate numbered 12 and 9 respectively, as compared with an expected frequency of 6.73 for each of these two ordinal positions. Now, out of 75 mental defectives, 8 were diagnosed as having *mongolism*, and 7 of these came from sibships having four or more members. Of these 7 mongols, 5 were last born children and two penultimate.

7. Distribution of patients in relation to sex of siblings (tables XXIII–XXV)

Table XXIII shows suggestive slight excesses of the total numbers of siblings of the same sex as the patient, in the case of psychneuroses, alcoholism and "other diagnoses", but these findings are of questionable significance.

Table XXIV fails to reveal any significant deviations from expected frequencies with which siblings were all the same sex as the patient or all of the opposite sex.

Table XXV shows that the sexes of siblings preceding and following the patient appear to differ significantly from expectation in the case of intermediate patients with psychoneuroses, and maybe so in the case of schizophrenics located in intermediate ordinal positions.

Discussion

1. Socio-cultural characteristics and median age at marriage

Previous investigations have shown high rates of first admission to mental hospitals in Western Ontario (*Wanklin et al.*, 1955), in Canada as a whole (*Gregory*, 1958 [c]) and elsewhere (e.g. *Malzberg*, 1940), among those with limited education; among the single, widowed and divorced; and among the foreign born. To whatever extent these rates reflect differences in incidence, it appears likely that the latter are related more to *selection* (on the basis of established abnormality or predisposition) than to *protection* (against precipitating stress or deprivation). Other studies suggest that prospects of leaving hospital and remaining in the community are least in the same groups that have the highest first admission rates (e.g. *Norris*, 1956; *Morgan and Johnson*, 1957).

The numerical distribution of the 1,000 patients in the present study, according to their main socio-cultural characteristics, is compatible with

these established differences in vulnerability among different groups of the general population.

In view of lower rates of marriage, and of fertility (e.g. *Lewis*, 1958) in certain diagnostic categories (particularly mental defectives and male schizophrenics), one might also expect to find some elevation in the median age at marriage. No gross difference in the latter is apparent in table VIII, but the numbers of married mental defectives and male schizophrenics in the sample were relatively small.

2. Surgical history

The surgical history of psychiatric patients may be of interest for several reasons, not the least of which is that consistent differences between the experiences of different diagnostic groups would appear to reflect valid distinctions between the clinical psychiatric diagnoses themselves. Now the main findings recorded in table VIII are a higher than average frequency of surgical operations in psychoneurotic patients of both sexes, and lower than average frequencies in mental defectives and foreign born schizophrenics. While these findings refer only to surgical operations, they appear to be somewhat at variance with the results of a careful study of the total physical illness history in patients with a variety of psychiatric disorders undertaken by *Lovett Doust* (1952). The latter author recorded histories of 38 bodily complaints and 72 somatic diseases in 272 psychiatric patients and 354 healthy adult controls, and found that the physical illness experience of the psychiatric patients was significantly in excess of that of the controls, psychotics having a heavier loading of previous physical illness than neurotics or psychopaths. Since patients and controls were each derived from two sources (part military and part civilian) the various diagnostic groups differed greatly from each other with respect to age and sex distribution; neurotics and psychopaths being predominantly young adult males, while the psychotics were older and contained high proportions of female patients (for both of which reasons the latter might be expected to have a higher physical illness history). *Lovett Doust* therefore carried out an analysis of variance, and concluded from his results that the influence of age and sex was insignificant in comparison with that of psychiatric diagnosis. However, it is necessary to add that the *total numbers* of neurotic and psychopathic *females* involved were very small (being 10 and 4 respectively).

A relatively higher frequency of physical illnesses and/or surgical operations in certain diagnostic groups than in others might reflect a selective factor in history taking, and it is considered quite possible that less information might be recorded concerning foreign born schizophrenics

(and possibly also some mentally defective patients) on account of difficulty in communication or inaccessibility of reliable informants. However, there is little reason to believe that the completeness of surgical histories obtained for psychoneurotics differed greatly from that of histories obtained for other diagnostic groups, and in all cases these surgical histories were supplemented by observations of operative scars made during physical examination. It, therefore, appears that there is a statistical association between psychiatric diagnosis and frequency of surgical operations. This might reflect a related constitutional predisposition to both physical and psychiatric disorder (e.g. *Lovett Doust*. 1952), or a direct causal connection between the two. Thus *Zwerling et al.* (1955) have discussed several types of relationship which they observed between emotional disorder and surgical illness in 200 patients randomly selected from the surgical wards of a public general hospital. They recorded 6 cases in which neurotic disorder simulated surgical illness, and 39 other cases where psychological factors appeared to result in behaviour producing surgical illness. In 6 cases psychological factors were believed to have contributed etiologically to tissue changes, and in 52 cases psychological factors apparently aggravated pre-existing or concomitant surgical illness. It may also be mentioned that in another study of psychiatric patients who had undergone thyroidectomy, *Quintanella* (1955) concluded that in almost every case for whom information was available, the onset of mental illness preceded the treatment of the thyrotoxicosis.

3. Frequency of abnormality in parents, full siblings and spouses

The frequencies of suicide and admission to mental hospital among *parents* and *full siblings* of psychotic patients appear to be higher than expected frequencies for the general population (e.g. *Kallmann*, 1950, 1952; *Fremming*. 1951), and are compatible with frequencies recorded in the relatives of psychotic patients (e.g. *Kallmann*, 1950, 1952; *Böök*, 1953).

The figure of 3.7 per cent admissions to mental hospital among the *spouses* of the youngest group of schizophrenic patients, by the time of the latter patient's admission to hospital, is suggestive, but requires confirmation in a larger sample of married patients.

4. Parental ages and age differences

It has long been known that *mongolism* is most frequent in the children of middle-aged parents and in the later birth ranks, and *Penrose* (1934) demonstrated that the most significant association is with advanced maternal age. There appear to be few studies of parental age in "functional" mental disorders, but *Barry* (1945) reported an undue frequency of

advanced maternal age for 1,000 state hospital patients, including 584 patients with dementia praecox, and 172 patients with manic depressive psychoses. *Norton* (1952) found a significantly higher proportion of 500 psychiatric patients (predominantly psychoneurotic) born to mothers at advanced ages, than of 500 matched physically ill controls. *Gregory* (1958 [a]) showed that the maternal age in *Norton*'s group exceeded the comparable figure for the general population, and also that there appeared to be some increase in median paternal age for the psychatric patients. The present study, however, shows no such finding for psychneurotic patients, but significant increases in the ages of both parents for schizophrenics and mental defectives.

The interpretation of data on parental ages may be extremely complex, and the same observations may have different explanations in different circumstances (e.g. *McKeown and Record*, 1956). Thus, mean parental ages may vary according to time, place, socio-economic status and a number of other factors. *Penrose* (1955) has discussed changes in mean parental ages which may be expected in disorders due to gene mutations. *Turnbull and Baird* (1957) have established that impaired foetal oxygenation is related to advanced maternal age, while *Hollingshead and Redlich* (1958) note a tendency for males from the lowest socio-economic class to marry late and to be considerably older than their wives.

Part of the increased parental ages for mental defectives, noted in the present study, is probably attributable to mongolism and may well be related to impaired foetal oxygenation. However, it is also known that the frequencies of both schizophrenia and mental deficiency are inversely related to socio-economic status, and the increased parental ages in these two diagnostic groups may well be at least partly related to socio-economic status rather than to psychiatric diagnosis. This possible relationship was not demonstrated in the present study, but it was established that parental age differences in the youngest group of schizophrenic patients were related extremely significantly to the duration of the patient's own education.

5. Loss of parents by death or permanent separation during childhood

In a recent review of studies on parental deprivation in psychiatric patients (*Gregory*, 1958 [b]), the present author attempted to discuss systematically various difficulties that have been encountered in studies of this nature, and to distinguish between reasonable probability and speculation concerning data hitherto recorded. Considerable evidence has accumulated that indicates an unusually high frequency of both parental deaths and separation during the early childhood of persons who

subsequently adopt delinquent, anti-social or psychopathic types of behaviour (e.g. *Glueck and Glueck*, 1950; *Bowlby*, 1952). The evidence has hitherto been inconclusive (i) that an increased frequency of parental deprivation is also associated with other forms of mental disorder, (ii) that the loss of mother is necessarily more significant than the loss of father, (iii) that observed associations indicate direct causal connections between parental deprivation and subsequent anti-social behaviour or other abnormalities.

However, certain studies point to an increased frequency of parental deprivation during childhood (both by death and separation) in psychoneuroses and the functional psychoses. Thus, *Barry* (1949) found an increased frequency of *maternal* deaths before the age of eight in 1683 psychotic patients (believed to be predominantly schizophrenic). *Norton* (1952) recorded an increased frequency of *paternal* deaths before the age of ten years, in 500 psychiatric patients (predominantly psychoneurotic). Data originally recorded by *Oltman et al.* (1952), and subjected to further analysis by *Gregory* (1958 [b]), showed relative increases in the frequency of parental deprivation (from all causes combined) by the age of seven years for the diagnoses dementia praecox, psychoneurosis and psychopathic personality (–and also showed an increased frequency of *paternal* deprivation among the neurotic group). In another recent article, *Oswald* (1958) investigated a series of young air force men, and found significantly more psychiatric cases had a history of parental deprivation than cases referred on account of isolated epileptic attacks.

The data presented in the present article (table XVI) appear to corroborate and extend the studies just quoted. Thus, loss of the father by death before the age of ten exceeded the expected frequency for the youngest schizophrenic group, for manic depressive psychoses and psychoneuroses, while loss of the mother by death before the age of ten exceeded the expected frequency for all schizophrenic groups.

Loss of a first parent by death alone involved the loss of father more frequently than mother in most diagnoses, and permanent loss of a first parent from all causes involved the loss of father more frequently than mother for all diagnoses. Figures for loss of a first parent by permanent separation (which included illegitimacy) were suggestively high for several diagnoses, but loss of a second parent by permanent separation in all instances exceeded the figure expected on the basis of figures for loss of a first parent of either sex. It, therefore, appears likely that for all diagnoses there were a number of instances in which there was a causal connection between the loss of the first parent (for whatever reason) and permanent separation from the second parent. In patients with mental deficiency, loss

of the second parent occurred almost twice as frequently, and in patients with pathological personality almost five times as frequently, as expected on the basis of frequencies of loss of a first parent of either sex (with the remaining diagnostic groups occupying intermediate positions).

These observations require further confirmation and extension in large series of patients, and should if possible be related to figures for parental deprivation in different social classes of the general population. However, their pattern suggests that, at least in certain diagnostic groups, there may well be causal relationships between parental deprivation and subsequent psychiatric disorder.

6. Size of sibship, birth order and ordinal position

(a) Size of sibship

Lewis (1958) recently published an extensive review of studies on fertility and mental illness, and concluded that patients with manic depressive psychoses have approximately normal fertility, while schizophrenics have much lower fertility than normal, largely because of lessened capacity for marriage. Little is known of the fertility of people with neurotic disorders, but there is no evidence that it differs greatly from the normal.

Almost all the studies reviewed by *Lewis* refer to the patient's *family of procreation*, rather than his family of orientation or origin. Attempts to examine *the size of the sibship or family of origin* have been confined to estimates of mean size, which have usually been biased in the manner described by *Greenwood and Yule* (1914). However, the latter authors calculated the corrected mean size of family of origin for Heron's heterogenous group of insane patients, and obtained a figure of 4.17, which would appear unduly low for children of British parents married a considerable time before the end of the nineteenth century. *Gregory* (1958 [a]) examined the corrected mean and distribution of family sizes for several groups of psychiatric patients on whom data had been recorded by two previous investigators, and it appeared that *Malzberg's* patients with dementia praecox came from unduly small families (in relation to their probable socio-economic status), or his manic depressives from unduly large families, or possibly both.

The latter findings do not correspond with those of the present study, in which the mean sizes of family of origin (for apparently legitimate patients) are all compatible with figures for the general population (bearing in mind that patients with manic depressive psychoses and psychoneuroses tend to be of higher socio-economic status than other diagnostic groups and

would therefore be expected to come from slightly smaller families).

With a relatively low mean size of family, a relatively high percentage of *only children* should be expected, but empirical observations of many distributions of family sizes (*Gregory*, 1958 [a]) appear to indicate that families with only one child are not usually the most frequent family size, when the mean is in excess of 2.6. The figures in table XX indicate that an unduly high proportion of the patients with manic depressive psychoses, psychoneuroses and pathological personality were only children (as was previously found with respect to *Norton's* psychoneurotic patients – *Gregory*, 1958 [a]). The possibility must be borne in mind that some of those recorded as legitimate only children were in fact illegitimate, but every attempt was made to exclude the latter. If valid, this finding is suggestive of environmental factors operative during the development of the only child.

(b) Birth order

A purely genetic hypothesis of causation for any given mental disorder implies random distribution of the disorder among different birth ranks and ordinal positions, irrespective of the sex of siblings or intervals between them and the patient.

Greenwood and Yule (1914) failed to discover any appreciable inequality between observed and expected frequencies of the various birth ranks among Heron's heterogenous group of insane patients. Subsequent studies by *Malzberg* 1940). *Norton* (1952) and *Böök* (1953), have also failed to establish any association between birth order and various funtional mental disorders. Data examined in the present study (table XXI) support these findings in failing to reveal any such association.

(c) ordinal position

Adler (quoted by *Ansbacher and Ansbacher*, 1956), and others have recorded their clinical impressions regarding the supposed vulnerability of some particular ordinal position. Most previous investigators of this problem have examined percentage distributions of cases among various ordinal positions, which are partly dependent on the percentage distribution of family sizes in the samples, and therefore provide no dignificant information on ordinal position per se. However, *Grosz and Miller* (1958) have recently published a satisfactory statistical study of ordinal position in 156 schizophrenics having only 2 liveborn siblings, as a result of which they

concluded that no ordinal position appears to carry specific vulnerability to schizophrenia within the three-sibling constellation. *Grosz* (1958) also reports that neither separation from one or other parent, nor age difference between the siblings in this group, was weighted in favour of either eldest, middle or youngest sibling.

Gregory (1958 [a]) compared observed and expected frequencies of various ordinal positions on data previously recorded by two other authors, and found significant excesses of observed frequencies of youngest children from families containing four or more members, most marked for two groups of psychotic patients. He discussed a number of possible sources of statistical error that might be responsible for these findings, and it now appears, in the light of negative findings in the present study, that either (a) the samples previously examined were in fact biased in the manner of their selection and/or recording, or (b) that the numbers of patients in comparable diagnostic groups in the present study were not sufficient to reveal significant differences. Indeed, in the present study, the only probably significant differences between expected and observed frequencies according to ordinal position were found for the patients with mental deficiency, and are probably attributable to the mongols included in this group.

7. *The sexes of siblings*

Adler (viz. *Ansbacher and Ansbacher*, 1956) postulated that emotional disorders were related to the unique position of the individual in the family of orientation, with respect to ordinal position and also the sexes of siblings. However, his impressions hitherto lack statistical confirmation.

While it is recognized that the numbers of patients in the separate diagnostic groups considered in the present study may not be sufficiently large, no very significant findings emerged with respect to the total numbers of siblings of either sex (table XXIII), or the frequencies of patients having all their siblings of the same sex as themselves, or all of the opposite sex (table XXIV). However, the findings with respect to the sexes of siblings immediately preceding and following schizophrenic and psychoneurotic patients located in intermediate ordinal positions (table XXV) are probably significant. If confirmed in future studies, such findings would appear to provide strong evidence of post-natal environmental influence.

In conclusion it may be said that certain of the factual data recorded and analysed in the present study are strongly suggestive of early environmental influences in the etiology of various diagnostic groups of adult psychiatric patients, but that further intensive and extensive investigations are required.

Summary

Current views on the role of genetic factors in determining intelligence, mental deficiency and mental disorders, have been summarized. The need for further investigation into the relative influence of genetic and early environmental influences in the etiology of the "functional" psychoses, psychoneuroses and other personality deviations, has been emphasized.

In the present investigation, considerable factual data concerning 1,000 patients admitted to a Canadian Mental Hospital have been recorded and analysed.

The distribution of these patients according to their main socio-cultural characteristics appears compatible with those recorded in previous studies, and no significant findings were established with respect to median age at marriage.

The recorded frequency of surgical operations was significantly higher than average in both male and female psychoneurotics, and lower than average in mental defectives and foreign born schizophrenics. These findings have been discussed in the light of certain studies by other authors.

Median and mean parental ages were significantly increased in schizophrenics and mental defectives. In the latter group, biological factors may be largely responsible (as apparently in mongolism), but in both groups the extent of socio-cultural factors remains undetermined.

The frequencies of parental deprivation by death or permanent separation during childhood appeared to be consistent with certain findings recorded in previous studies. Loss of a father by death during early childhood was more frequent than expected in the youngest group of schizophrenics, in manic depressives and psychoneurotics. Loss of a mother by death during early childhood exceeded the expected frequency in all schizophrenic groups. Loss of father by permanent separation appeared unduly frequent in certain groups, and loss of a second parent by permanent separation occurred in various diagnostic groups from almost two to almost five times as frequently as expected from the frequencies with which they lost one parent of either sex. The pattern of these findings is considered suggestive of environmental influence, but requires further investigation.

The mean size of sibship was compatible with what is known of the socio-cultural characteristics of the various diagnostic groups, but only children were found unduly frequently among apparently legitimate patients with manic depressive psychoses, psychoneuroses and pathological personality.

There were no significant differences between observed and expected frequencies of each birth order for any diagnostic group. Mental deficiency

was the only diagnostic group in which certain ordinal positions (in families having four or more members) were found more frequently than expected, and this finding appeared to be attributable to the mongols included in the sample of mental defectives. Previously recorded significant findings with respect to ordinal position (*Gregory*, 1958 [a]) may well have been due to sampling errors.

The sexes of siblings immediately preceding and following patients with schizophrenia and psychoneuroses were not distributed according to expectancy, and these findings are suggestive of environmental influence, but await confirmation.

It is concluded that some of the factual data recorded and analysed in the present study strongly suggest early environmental influences in the etiology of various diagnostic groups of adult psychiatric patients, but that considerable further data must be recorded and subjected to critical evaluation.

Zusammenfassung

Es werden die häufigsten Ansichten darüber zusammengefaßt, inwieweit genetische Faktoren bei der Entwicklung von Intelligenz, Geisteskrankheiten und Geistesstörungen eine Rolle spielen. Besonders hervorgehoben wurde die Notwendigkeit weiterer Untersuchungen über den relativen Einfluß von Erbanlagen und frühen Umwelteinflüssen in der Ätiologie der funktionellen Psychose, Psychoneurose und anderer Persönlichkeitsveränderungen.

Bei der vorliegenden Untersuchung wird umfangreiches Material über 1000 Patienten des Canadian Mental Hospitals aufgeführt und ausgewertet.

Die Verteilung der Patienten nach ihrem hauptsächlichen soziologisch-kulturellen Hintergrund scheint mit dem übereinzustimmen, was frühere Untersuchungen gezeigt haben, und hinsichtlich ihres durchschnittlichen Heiratsalters wurden keine signifikanten Feststellungen gemacht.

Die Zahl der chirurgischen Eingriffe war sowohl bei männlichen als auch bei weiblichen Psychoneurotikern beträchtlich höher als gewöhnlich und im Durchschnitt niedriger bei Schwachsinnigen und bei im Ausland geborenen Schizophrenen. Diese Resultate wurden diskutiert und mit den Studien anderer Autoren verglichen.

Bei Schizophrenie und Schwachsinn ist das elterliche Alter beträchtlich erhöht. In der letzten Gruppe mögen biologische Faktoren weitgehend mitbestimmend sein (wie offenbar beim Mongolismus), jedoch bleibt in beiden Gruppen das Ausmass des soziologisch-kulturellen Faktors unbestimmt.

Die Häufigkeit eines Verlustes der Eltern durch Tod und ständige Trennung während der Kindheit scheint gewissen Zahlen früherer Untersuchun-

gen zu entsprechen. Ein Verlust des Vaters durch Tod in der frühen Kindheit war häufiger als erwartet in der jüngsten Gruppe Schizophrener, Manisch-Depressiver und der Psychoneurotiker. Der Tod der Mutter in früher Kindheit überstieg die erwartete Häufigkeit in allen schizophrenen Gruppen. Ein Verlust des Vaters durch ständige Trennung trat in gewissen Gruppen besonders oft auf, und zu dem Verlust eines zweiten Elternteiles durch ständige Trennung kam es in verschiedenen diagnostischen Gruppen etwa 2–5 mal so oft, als auf Grund der Häufigkeit, mit der die Patienten einen Elter verloren, erwartet wurde. Diese Ergebnisse zusammengenommen weisen offenbar auf Umwelteinflüsse hin, machen jedoch weitere Untersuchungen erforderlich.

Die mittlere Grösse der Geschwisterschaft entspricht dem, was über die soziologisch-kulturellen Eigenarten der verschiedenen diagnostischen Gruppen bekannt ist; aber unter den offenbar ehelich geborenen Patienten mit manisch-depressiven Psychosen, Psychoneurosen und Psychopathien wurden Einzelkinder ungewöhnlich häufig gefunden.

Es gab keine signifikanten Unterschiede zwischen beobachtetem und erwartetem Auftreten jeder Geburtennummer für irgendeine diagnostische Gruppe. Schwachsinn war die einzige diagnostische Gruppe, in der gewisse Geburtennummern (bei Familien mit 4 oder mehr Personen) häufiger als erwartet festgestellt werden konnten; und diese Feststellung war offenbar auf die Mongoloiden zurückzuführen, die in der Stichprobe von Schwachsinnigen enthalten waren. Früher aufgezeichnete signifikante Ergebnisse in Hinsicht auf die Geburtennummer werden wohl auf Irrtümern in der Stichprobenerhebung beruhen.

Das Geschlecht der Geschwister, denen Patienten mit Schizophrenien und Psychoneurosen direkt vorangehen und folgen, war nicht zufällig verteilt; diese Ergebnisse deuten auf den Einfluß der Umwelt hin, müssen jedoch noch bestätigt werden.

Es wird geschlossen, daß einige der in der vorliegenden Arbeit aufgeführten und untersuchten Tatsachen auf frühe Einflüsse der Umwelt in der Ätiologie verschiedener diagnostischer Gruppen erwachsener psychiatrischer Patienten hinweisen, daß jedoch noch viele andere Daten gewonnen und kritisch überprüft werden müssen.

Résumé

L'auteur donne tout d'abord une vue d'ensemble des opinions actuelles sur le rôle des facteurs génétiques dans l'intelligence, l'oligophrénie et les troubles mentaux. Il relève surtout l'importance d'investigations futures pour déterminer la part qui revient à l'influence de facteurs génétiques et

à celle du milieu ambiant dans l'étiologie de psychoses «fonctionnelles», de psycho-névroses et d'autres déviations de la personnalité.

Le présent travail comprend une analyse des données de 1000 patients admis à un hôpital psychiatrique canadien.

La répartition sociale et culturelle de ces malades correspondait à celle trouvée dans d'autres études analogues et, en particulier, l'âge moyen du mariage ne déviait pas de la normale. La fréquence d'opérations chirurgicales était significativement plus élevée chez les hommes et les femmes névrosés que dans la moyenne; d'autre part, chez les oligophrènes et les schizophrènes nés à l'étranger elle était plus basse que dans la moyenne.

L'âge parental médian et moyen était très augmenté chez les schizophrènes et les oligophrènes. Dans le dernier groupe des facteurs biologiques peuvent en être largement responsables (comme par exemple dans le mongolisme), mais dans les deux groupes la portée des facteurs sociaux et culturels reste encore indéterminée.

La mort ou la séparation des parents pendant l'enfance se sont révélées également d'une certaine importance correspondant aux résultats notés par d'autres auteurs. Le décès du père au cours de la première enfance était significativement plus fréquent dans le groupe le plus jeune des schizophrènes, chez les maniaco-dépressifs et chez les sujets névrosés. Le décès de la mère au cours de la première enfance dépassait la fréquence attendue dans tous les groupes de schizophrènes. La perte du père par séparation permanente apparaissait très élevée dans certains groupes, alors que la perte des deux parents par séparation permanente survenait dans les divers groupes avec une fréquence 2 à 5 fois plus élevée que celle relevée pour la perte d'un seul parent. Ces données suggèrent une certaine influence du milieu ambiant, mais nécessitent encore des investigations approfondies.

La dimension moyenne d'une fratrie correspondait aux données sociales et culturelles des différents groupes, mais une fréquence accrue d'enfants se trouvait seulement parmi les malades atteints de psychoses maniaco-dépressives, de psycho-névroses et de personnalités pathologiques.

On ne notait pas de différence significative entre fréquence observée et attendue dans l'ordre de naissance des malades de chaque groupe étudié. L'oligophrénie était le seul groupe dans lequel certaines déviations de la parité ont été trouvées plus fréquentes qu'escomptées. Ce résultat doit être mis sur le compte des mongols qui ont été inclus dans le groupe des oligophrènes.

La répartition des sexes des enfants précédant ou suivant les malades avec schizophrénie ou névrose ne correspondait pas à l'attente théorique, ce qui suggère une influence du milieu ambiant, mais doit encore être confirmé.

L'auteur conclut que les données analysées dans ce travail indiquent une influence du milieu ambiant pour l'étiologie de différentes formes de maladies mentales, mais qu'il faut encore rassembler un matériel considérable pour pouvoir évaluer de façon critique ces résultats.

ACKNOWLEDGEMENTS

I am grateful to Dr. B. H. McNeel, Chief of the Mental Health Division, Ontario Department of Health, and to Dr. A. McCausland, Medical Superintendent of the Ontario Hospital, London, Canada, for the time and opportunity to carry out this investigation, and for permission to publish data on the patients involved. I am also indebted to many members of the hospital staff who recorded the information without which the present analysis would not have been possible.

REFERENCES

Ansbacher, H. L. and Ansbacher, R. R.: The individual psychology of Alfred Adler, pp. 376 to 382. (Basic Books, New York 1956.)

Barry, H., Jr.: Arch. Neurol. Psychiat., Chicago *54:* 186 (1945).

Barry, H., Jr.: Arch. Neurol. Psychiat., Chicago *62:* 630 (1949).

Böök, J. A.: Acta genet. *4:* 71 (1953).

Bowlby, J.: Maternal care and mental health, W. H. O. Monogr. Ser. No. 2 (1952).

Burt, C.: Eugen. Rev., *49:* 137 (1957).

Dominion Bureau of Statistics. 8th decennial Census of Canada, 1941. Vol. *3*, table 52. (Edmond Cloutier, Ottawa. 1941.)

Dominion Bureau of Statistics. Vital Statistics, 1951. Table 20. (Edmond Cloutier, Ottawa 1951.)

Fremming, K. H.: The expectation of mental infirmity in a sample of the Danish population. Occ. Pap. Eugen., No. 7. (Eugenics Society and Cassell & Co. Ltd., London 1951.)

Glueck, S. and Glueck, E.: Unraveling juvenile delinquency, pp. 122–124. (Harvard Univ. Press, Cambridge, Mass. 1950).

Greenwood, M., Jr., and Yule, G. U.: J. roy. statist. Soc. *77:* 179 (1914).

Gregory, I.: Brit. J. prev. soc. Med., *12:* 42 (1958 [a]).

Gregory, I.: Amer. J. Psychiat., *115:* 432 (1958 [b]).

Gregory, I.: First admission rates to Canadian mental hospitals, III., Canad. Psychiat. Ass. J., in press. (1959).

Grosz, H. J.: Personal communication (1958).

Grosz, H. J. and Miller, I.: Science *128:* 30 (1958).

Hollingshead, A. B. and Redlich, F. C.: Social class and mental illness, pp. 126 and 1555–165 (1958).

Kallmann, F. J.: The genetics of psychoses, In Congr. int. Psychiat. Paris 1950. Vol. *6:* Psychiatrie sociale – génétique et eugénique, Rapports, p. 1 (Hermann, Paris 1950).

Kallmann, F. J.: Genetic aspects of psychoses, In The biology of mental health and disease, p. 283, 27th Ann. Conf. Milbank Memorial Fund (New York 1952).

Kallmann, F. J.: Heredity in health and mental disorder. (Norton, New York 1953).

Kallmann, F. J.: The genetics of psychotic behaviour patterns, In Genetics and the inheritance of integrated neurological and psychiatric patterns, p. 357, Res. Publ. Ass. nerv. ment. Dis., Vol. *33* (Williams & Wiklins, Baltimore 1954).

Larsson, T. and Sjögren, T: Acta psychat. scand., Suppl. 89, p. 139 (1954).

Lewis, A.: Eug. Rev. *50:* 91 (1958).

Lovett Doust, J. W.: Brit. J. soc. Med. *6:* 49 (1952).

Malzberg, B.: Social and biological aspects of mental disease (State Hospitals Press, Utica, N. Y. 1940).

McKeown, T. and Record, R.G.: Amer. J. hum. Genet. *8:* 8 (1956).

Morgan, N. C. and Johnson, N. A.: Amer. J. Psychiat. *113:* 824 (1957).

Neel, J. V. and Schull, W. J.: Human heredity, p. 277, (Univ. Chicago Press, Chicago 1954).

Norris, V.: J. ment. Sci. *102:* 467 (1956).

Norton, A.: Brit. J. soc. Med. *6:* 253 (1952).

Oltman, J. E.; McGarry, J. J. and Friedman, S.: Amer. J. Psychiat. *108:* 685 (1952).

Oswald, I.: Brit. med. J., *i:* 1515 (1958).

Penrose, L. S.: Proc. roy. Soc. B. *115:* 431 (1934).

Penrose, L. S.: J. ment. Sci. *90:* 399 (1944).

Penrose, L. S.: Research methods in human genetics, In Congr. Psychiat. Paris 1950. Vol. *6:* Psychiatrie sociale – génétique et eugénique, Rapports, p. 41 (Hermann, Paris 1950).

Penrose, L. S.: Lancet, *ii:* 312 (1955).

Quintanella, J.: Dis. nerv. Syst. *16:* 1 (1955).

Registrar-General for Ontario, Annual Reports relating to the registration of births, marriages and deaths, in the Province of Ontario, for the years 1921, 1931, 1941 and 1951. (The Queen's printers, Toronto 1951).

Roberts, J. A. F.: Proc. 7th int. Genet. Congr., p. 249 (1941).

Roberts, J. A. F.: The genetics of oligophrenia, In Congr. int. Psychiat. Paris 1950. Vol. *6:* Psychiatrie sociale – génétique et eugénique, Rapports, p. 55 (Hermann, Paris 1950).

Sjögren, T.: The genetics of schizophrenia, In IInd int. Congr. Psychiat. Zurich 1957. Synopses, p. 129.

Slater, E.: J. ment. Sci. *90:* 17 (1944).

Slater, E.: The genetical aspects of personality and neurosis, In Congr. int. Psychiat. Paris 1950. Vol. *6:* Psychiatrie sociale – génétique et eugénique, Rapports, p. 119. – (Hermann, Paris 1950).

Slater, E.: Psychotic and neurotic illnesses in twins, Med. res. Coun. spec. Rep. Ser., 278. (H. M. S. O., London 1953).

Turnbull, E. P. N. and Baird, D.: Brit. med. J., *ii* 1021 (1957).

Walker, N. F. and Reid, D. B. W.: Amer. J. Psychiat. *111:* 633 (1955).

Wanklin, J. M.; Fleming, D. F.; Buck, C. W. and Hobbs, G. E.: J. nerv. ment. Dis. *121:* 103 (1955).

Zwerling, I.; Titchener, J.; Gottschalk, L.; Levine, M.; Culbertson, W.; Cohen, S. F. and Silver, H.: Amer. J. Psychiat. *112:* 270 (1955).

Author's address: Ian Gregory, M.A., M.D., D. Psych., 318 Grosvenor St., *London*, Ontario (Canada) until June 14/59. Department of Psychiatry, University of Minnesota Medical School, *Minneapolis 14*, Minn. (U.S.A.) after June 14/59.

Increase Your Professional Effectiveness

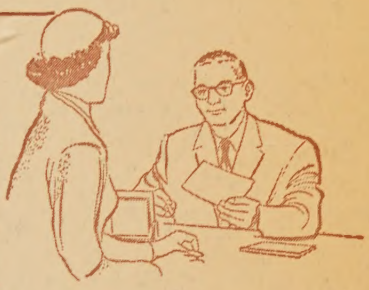
THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE

Official Organ—The American Roentgen Ray Society and The American Radium Society. Edited by Lawrence Reynolds. Comprehensive coverage of the latest developments in this increasingly important specialty. In each issue 10 to 15 original articles by recognized authorities. Price a year: United States, U. S. Possessions, Pan-American Union and Spain, $15.00; Canada, $16.00; other foreign countries, $17.00. Monthly.

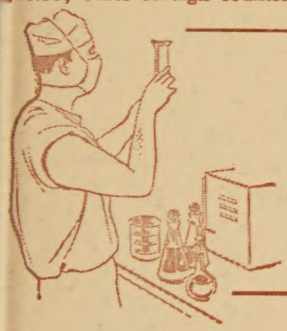
PEDIATRICS

Official Journal—American Academy of Pediatrics. Edited by Charles D. May. PEDIATRICS supplies advances in pediatrics that are applicable to daily work. Comprehensive coverage of all phases of child development and the treatment of children's diseases. Price a year: United States, U. S. Possessions, Pan-American Union and Spain, $12.00; Canada, $13.00; other foreign countries, $14.00. Monthly.

THE JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM



Official Journal—The Endocrine Society. Editor-in-Chief: Alexander Albert; Managing Editor, Phebe K. Thompson. A medium of publication preferred by foremost investigators and clinical authorities for the publication of their work in practical endocrinology. Stresses current clinical and laboratory methods. Price a year: United States, U. S. Possessions, Pan-American Union and Spain, $15.00; Canada, $15.50; other foreign countries, $16.00. Monthly.



ENDOCRINOLOGY

Official Journal—The Endocrine Society. Edited by Roy O. Greep. Well-informed investigators depend on this journal for a complete accounting of progress in endocrinology and associated fields. Ten to twelve original articles in each issue. Specific information on new and standard endocrine products and materials. Price a year: United States, U. S. Possessions, Pan-American Union and Spain, $15.00; Canada, $15.50; other foreign countries, $16.00. Monthly.

JOURNAL OF NEUROSURGERY

Official Journal—The Harvey Cushing Society. Edited by Louise Eisenhardt. Read by leading neurosurgeons of the world. The steady growth of neurological surgery as a specialty is readily apparent in this beautifully produced journal which publishes articles relating primarily to neurosurgery. Price a year: United States, U. S. Possessions, Pan-American Union and Spain, $11.00; Canada, $11.50; other foreign countries, $12.00. Bi-monthly.

JOURNAL OF NEUROPHYSIOLOGY

Editorial Board: John F. Fulton, Stephen W. Kuffler, Paul D. Maclean, H. W. Magoun, James L. O'Leary, Theodore C. Ruch, Donal Sheehan, Clinton L. Woolsey. For a decade the principal avenue of publication for the continuously increasing stream of meritorious contributions in neurophysiology. Price a year: United States, U. S. Possessions, Pan-American Union and Spain, $9.50; Canada, $10.00; other foreign countries, $10.50. Bi-monthly.

CHARLES C THOMAS • PUBLISHER • 301-327 East Lawrence Avenue • SPRINGFIELD • ILLINOIS

EUGENICS QUARTERLY

Vol. 5, No. 4 December, 1958

CONTENTS:

Contributed Articles Welcome

Published by

AMERICAN EUGENICS SOCIETY

230 Park Avenue New York 17, N.Y.

Subscription: $5.00 — Membership: $5.00 — (Foreign: $2.50)